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PART I
REACTIONS OF ENOLATES DERIVED FROM
UNSYMMETRICAL CYCLIC KETONES

PART II
PHOTOCHEMICAL REARRANGEMENTS OF
CROSS CONJUGATED CYCLOHEXADIENONES
RELATED TO INDAN

A THESIS

Presented to

The Faculty of the Graduate Division

by

William Joseph Powers, III

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May, 1968

PART I

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Approved:

Chairman

Date approved by Chairman: May 27, 1968

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GLOSSARY OF ABBREVIATIONS

DME	1, 2-dimethoxyethane
DDHQ	2, 3-dicyano-5, 6-dichlorohydroquinone
DDQ	2, 3-dicyano-5, 6-dichlorobenzoquinone
Dow 550	silicone oil (Dow Chemical Company)
Hz	Hertz
SE-30	silicone gum rubber (methyl)
TMS	tetramethylsilane, nmr standard
THF	tetrahydrofuran
vpc	vapor phase chromatography

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PART I

CHAPTER I

INTRODUCTION

Alkylation of enolates derived from ketones is an often employed method of forming a new carbon-carbon bond. Despite the wide use of this technique in synthetic organic chemistry, the method suffers several disadvantages, particularly when an unsymmetrical ketone is to be alkylated. One of the biggest drawbacks of direct base catalyzed alkylation of a ketone is that a complex mixture of mono and polyalkylated products is often formed, requiring difficult and often tedious separation of the desired alkylation product. This difficulty is shown in Chart I, using 2-methylcyclohexanone as a model compound (1). With triphenylmethylpotassium, initial enolate formation is irreversible (2). Enolization is most likely reversible with most weaker bases, such as potassium tert-butoxide and sodamide.

A second problem of direct base catalyzed alkylation which is particularly troublesome in the case of cyclopentanones is that of self condensation of the ketone to form dimers or large oligomers (3).

Many ingenious methods of directing alkylation to the desired position have appeared in the literature. These methods can generally be placed in four categories:

(1) Use of a blocking group at the unsubstituted alpha position which then forces the alkylating agent to react at the substituted position only. The blocking

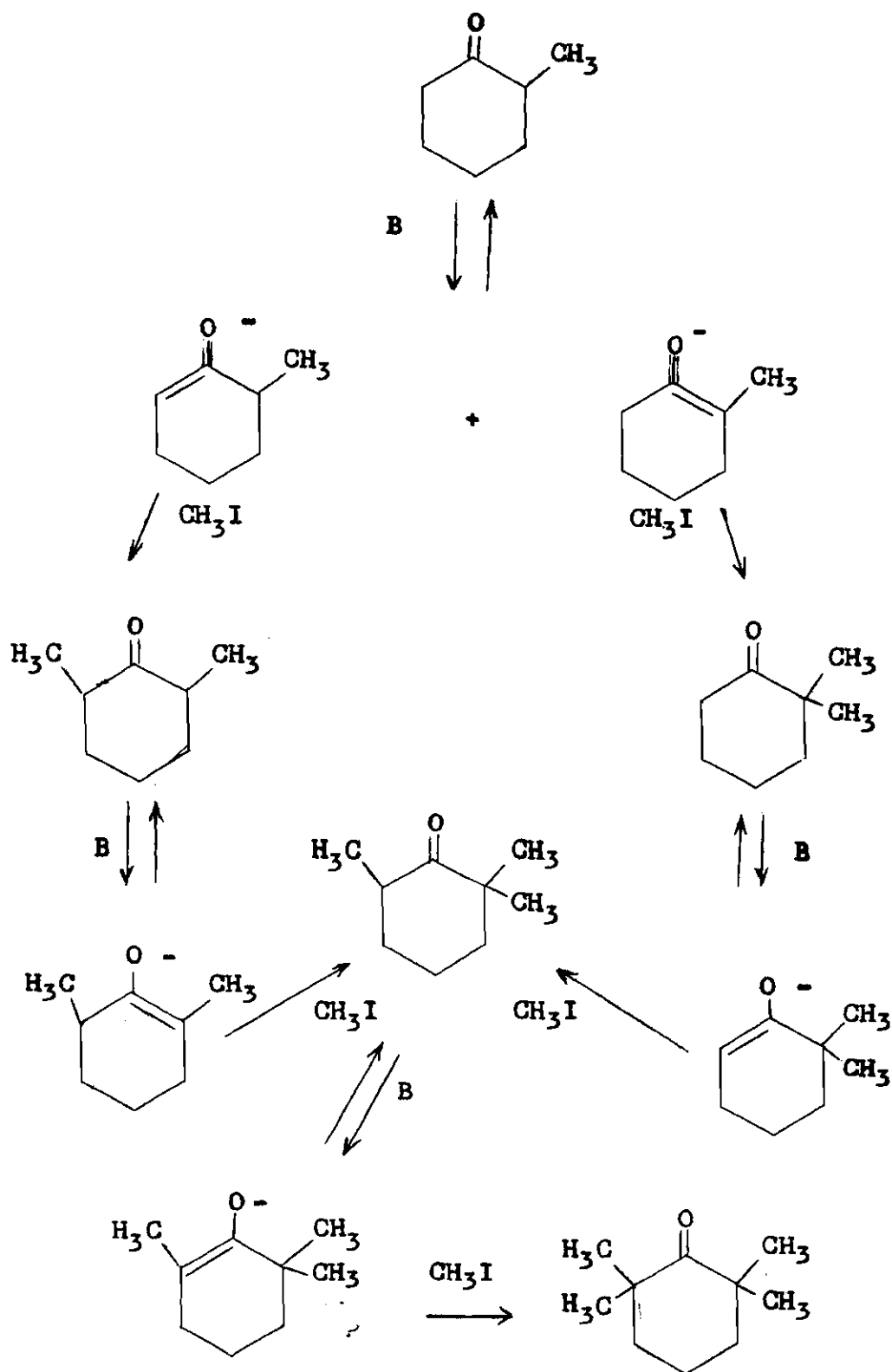


Chart 1. General Scheme for Direct Base Catalyzed Alkylation of a Ketone

group is then removed.

(2) Introduction of an electron withdrawing activating group at the unsubstituted alpha positions. This makes the activated position much more reactive and directs the alkylation to it. The activating group is then removed.

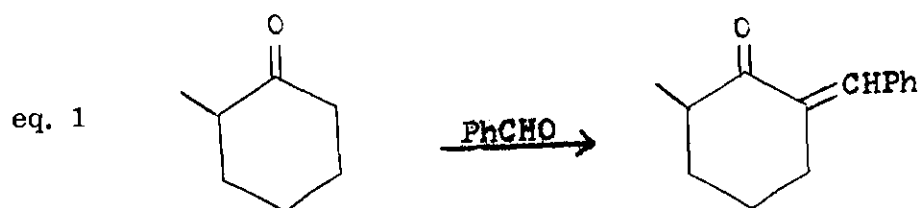
(3) The formation and alkylation of enamines and Schiff base anions.

(4) Reductive-alkylation methods.

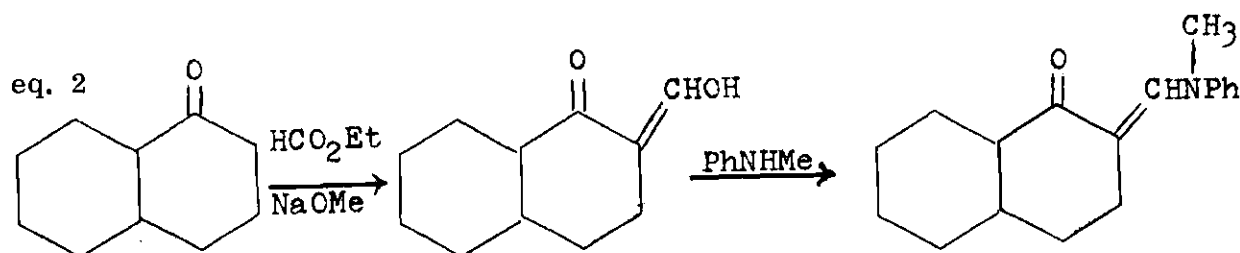
Methods 1 and 2 suffer from the serious disadvantage of requiring several steps in order to obtain the desired alkylation product. Method 3 has chiefly been applied to symmetrical ketones. Method 4 has the serious disadvantage that many of the compounds needed for reduction are difficult to synthesize.

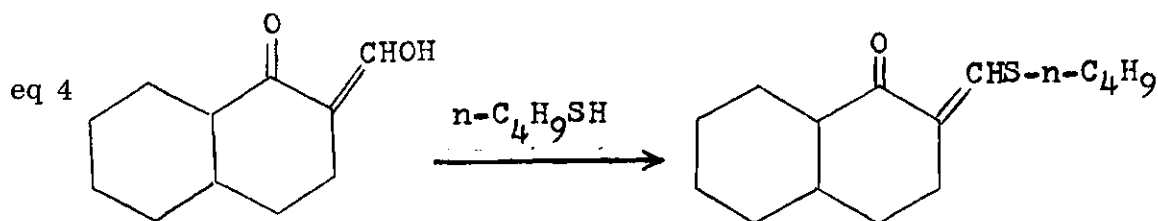
Specific examples of blocking groups include the benzylidene group (eq 1)

(4)



the aminated (eq 2) (5) or alkylated (eq 3) (6) formyl group and the thioether of a formyl group (eq 4) (7).

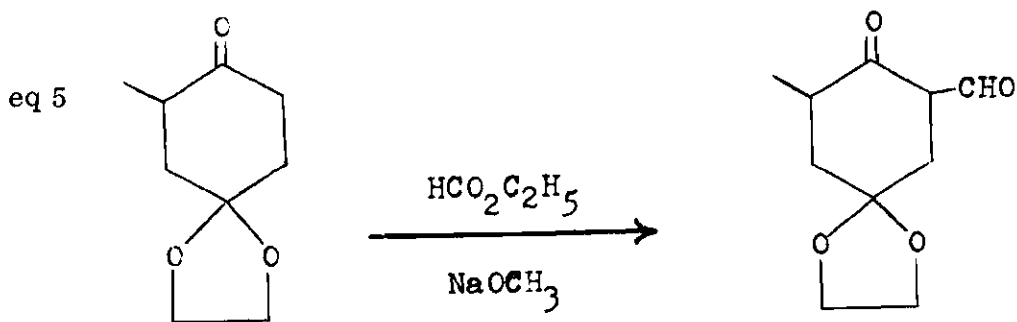




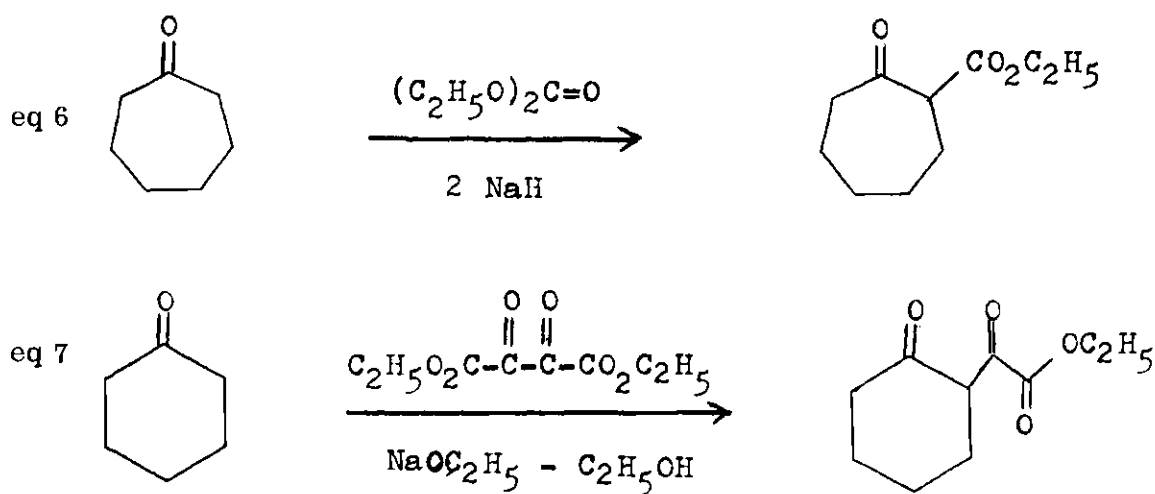
All of the products of equations 1-4 have been further reacted with a strong base and alkylating agent to give monoalkyl products with the alkylation occurring at the open alpha position. The blocking groups can then be removed. The above methods have the advantage of giving a relatively pure product monoalkylated at the desired position. However, the multistep processes involved are time consuming and overall yields are often low.

The groups most often used to activate an alpha position are the formyl, carbethoxyl and ethoxyalyl moieties (8).

Formylation can be accomplished by base catalyzed reaction of the ketone with ethyl formate as shown in Equation 5 (9).



Introduction of a carbethoxyl group can be accomplished by direct reaction of the ketone with diethyl carbonate (eq 6) (10) or by reaction of the ketone with diethyl oxalate followed by pyrolytic decarbonylation of the ethoxyalyl adduct (eq 7) (11). The latter method often gives better yields, despite the additional step, because of the higher reactivity of the oxalate ester.

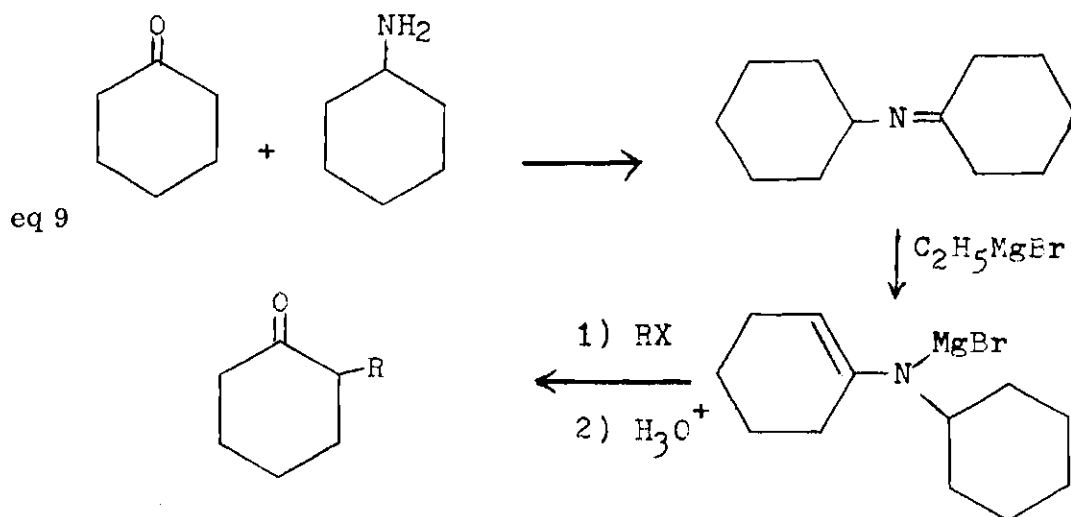
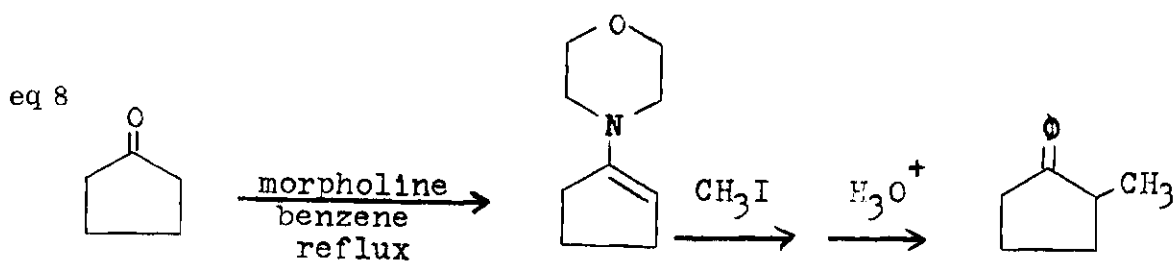


The ethoxyalyl group can itself be used as an activating group (12). The activated position is much more acidic than the unactivated position, resulting in the generation of a specific enolate upon reaction with base. After alkylation, the activating group is removed. Formyl and carbethoxyl groups can be removed hydrolytically: alkoxide solutions are used to remove the ethoxyalyl moiety.

The alkylation of enamines (13) and the anions of Schiff's bases (14) was developed by Stork and coworkers. Both of these methods have generally been applied to symmetrical ketones. Enamines are prepared by reaction of a ketone with a secondary amine. The enamines can be alkylated in reasonable good yield but when only moderately active alkylating agents, such as methyl iodide are

employed, conversion is not complete. An example of enamine formation and alkylation is given in Equation 8.

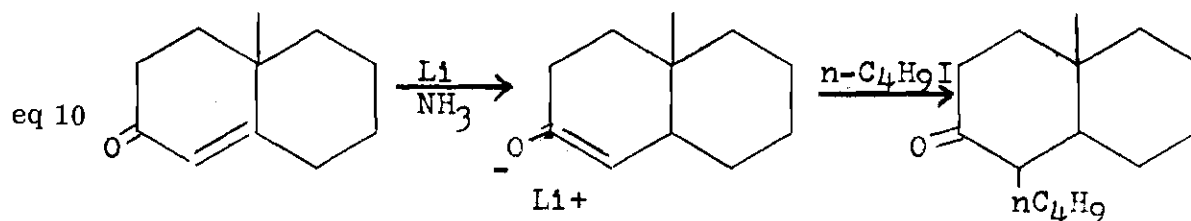
The preparation and alkylation of a Schiff's base anion is shown in Equation 9. This method is superior to enamine alkylation for moderately reactive alkylating agents.



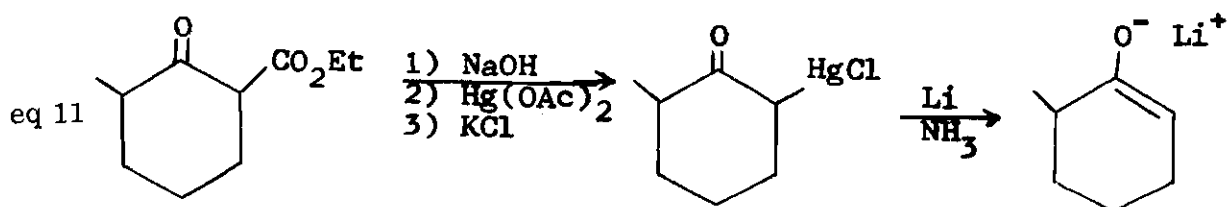
The procedure of reductive alkylation of enones was developed by Stork and coworkers (15) and has received some application. In this method shown in Equation 10 the enolate is generated by reaction of an enone with a solution of an

alkali metal, usually lithium, in liquid ammonia, then alkylated in this solvent.

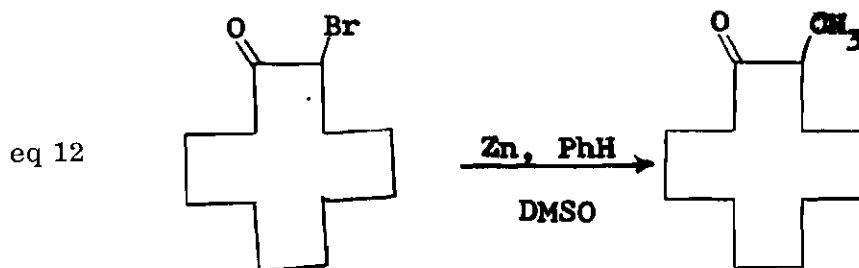
Lithium is generally chosen since the rate of alkylation of lithium enolates is faster than their rate of equilibration. Yields are improved by addition of a proton donor, such as tert-butyl alcohol (16).



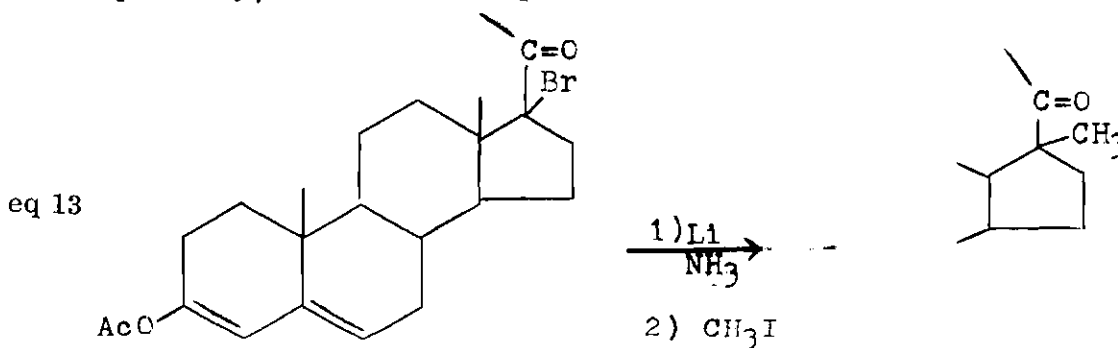
A second reductive method for the generation of a specific enolate is via reduction of an alpha chloromercuri ketone, as shown in Equation 11 (17). The enolate so generated is then alkylated. Little application of this method has been made.



A third reductive method was recently reported by Spencer and co-workers (18). Treatment of alpha-bromoketones with 10:1 mixtures of benzene: dimethyl sulfoxide (DMSO) in the presence of zinc metal results in replacement of the bromine with a methyl group as shown in Equation 12.



A fourth reductive method of alkylation has been reported by Weiss and co-workers (19). The steroidal enol acetate, 17-bromopregnenolone acetate, was treated with lithium in liquid ammonia to give the methylated enol acetate in nine percent yield as shown in Equation 13.



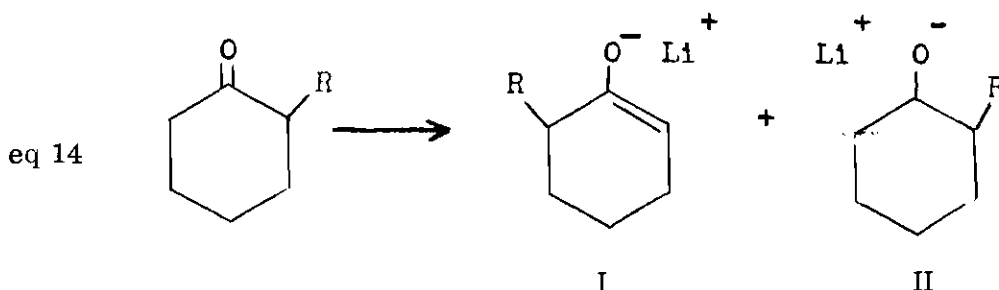
House and co-workers (12) and Caine (17) have extended the work of Stork (15) showing that lithium enolates possess certain properties that make them desirable for possible specific alkylation:

(1) Under kinetic conditions using excess triphenylmethyllithium as the base, the less substituted enolate (I) predominates over the more substituted enolate II (eq 14). This preference is greater than in the case of potassium enolates.

(2) The kinetic lithium enolate mixture equilibrates much more slowly

than the corresponding potassium enolate mixture and reacts with trapping reagents much more rapidly than it equilibrates.

(3) At equilibrium, the more substituted lithium enolate is generally favored over the less substituted enolate in the case of cyclic ketones (eq 14). This preference is larger in the case of lithium than for a corresponding mixture of potassium enolates.



The purpose of this research was to investigate the position of enolization of several unsymmetrical cyclic ketones as determined by trapping the enolate mixtures with acetic anhydride. In particular, a series of cyclohexanones was studied to evaluate steric effects on lithium enolate formation. 2-Methylcyclopentanone was also studied. The bases used to cause enolization were triphenylmethyllithium and triphenylmethylpotassium. These bases were chosen for this study because of their ability to completely convert ketones to enolate anions. The possibility of using lithium enolates to effect alkylation at a specific alpha position was also studied.

CHAPTER II

INSTRUMENTATION AND EQUIPMENT

Boiling points are uncorrected. Carbon and hydrogen microanalyses were performed by Galbraith Laboratories, Incorporated, Knoxville, Tennessee. Proton magnetic resonance spectra were recorded on a Varian, Model A-60, high resolution spectrometer, using carbon tetrachloride containing tetramethylsilane (TMS) as an internal standard as solvent. Chemical shifts are reported in ppm down field from the standard. The abbreviations s, d, t, q and m respectively refer to singlet, doublet, triplet, quartet and multiplet; coupling constants are reported in Hz. Catalytic hydrogenations were performed in a Parr low pressure reaction apparatus using 95 percent ethanol as the solvent. Solvent evaporations were carried out at reduced pressure using a commercial rotating evaporator. An Aerograph Manual Temperature Programmer Gas Chromatograph, Model A-90P was employed for all vapor phase chromatography (vpc) work. Commercial reagent grade triphenylmethane was used without further purification. Commercial 1,2-dimethoxyethane (DME) and tetrahydrofuran (THF) were purified by distillation through a five foot vacuum jacketed column packed with glass helices, then distilled from lithium aluminum hydride immediately prior to use. Anhydrous ether was stored over sodium ribbon and distilled from lithium aluminum hydride immediately prior to use. Liquid organic compounds were distilled prior to use. Reagent grade inorganic chemicals were used in this research.

CHAPTER III

EXPERIMENTAL

2-Ethylcyclohexanone (III)

The general method of Stork et al was employed (20) for the synthesis of III. Anhydrous ammonia, ca 500 ml, was distilled into a 3000 ml three-necked round-bottom flask fitted with a mechanical stirrer and dry ice condenser. Finely cut lithium wire 7.0 g (1.0 moles) was added and the mixture was stirred for 30 min. A solution of 31.0 g (0.254 moles) of ortho-ethylaniline in 50 ml of anhydrous tert-butyl alcohol was added. The reaction mixture was stirred for 2.5 hr and ca 500 ml of water was added. The reaction mixture was allowed to warm to room temperature, then saturated with salt and extracted with three 100 ml portions of ether. The ether extracts were combined and dried over anhydrous magnesium sulfate. The solvents were removed in vacuo. The resulting oil was added to 250 ml of ice cold five percent hydrochloric acid. The mixture was heated to 90°C over a 20 min period, then allowed to cool to room temperature. The layers were separated and the aqueous layer extracted with three 50 ml portions of ether. The combined organic layers were dried over anhydrous magnesium sulfate and the solvents removed in vacuo. The crude product, 12.0 g, was dissolved in ca 150 ml of 95 percent ethanol and 1.5 g of five percent palladium on charcoal was added. The mixture was placed on a Parr shaker under 40 psi of hydrogen for one hour. The solvents were removed in vacuo and the resulting oil was distilled

through a four inch Vigreux column to give 10.5 g (33 percent) of III, b. p. 78-80°C/22 mm Hg. (lit. 110°C/36 mm Hg (21))

o-Isopropylanisole (IV)

Compound IV was prepared by the general method of Gilman (30). A 1000 ml three-necked round-bottom flask was equipped with a mechanical stirrer, thermometer, and dropping funnel and charged with a solution of 45.5 g (0.81 moles) of potassium hydroxide in ca 500 ml of water. The solution was cooled to zero degrees with an ice salt bath and 110.2 g (0.81 moles) of o-isopropylphenol was added in one portion. Dimethyl sulfate, 102 g (0.81 moles) was added dropwise at a rate sufficiently slow to keep the temperature at or below zero degrees. The reaction mixture was kept at zero degrees for one hour after completion of the addition, then allowed to come to room temperature. The layers were separated and the aqueous layer was saturated with salt and extracted with three 100 ml portions of ether. The combined organic layers were dried over magnesium sulfate and the solvents were removed in vacuo. The resulting oil was distilled through a Claisen head, b. p. 105-107°C/23 mm Hg (lit. 122-4°C/18 mm (20)).

2-Isopropylcyclohexanone (V)

This compound was prepared by a modification of the method of Stork et al (20). Approximately 500 ml of liquid ammonia was distilled into a dried 3000 ml three-necked round-bottom flask fitted with a mechanical stirrer, dropping funnel, and dry ice condenser and under positive nitrogen flow. Finely cut

lithium wire, 14.0 g (2.1 moles) was added and the mixture was stirred for 30 min. A solution of 75.0 g (0.50 moles) of Compound IV in ca 200 ml of anhydrous tert-butyl alcohol was added dropwise over a ten minute period. The mixture was stirred for 2.5 hrs, then 1200 ml of water was added as rapidly as possible. The reaction mixture was allowed to warm to room temperature and saturated with salt. The aqueous and organic layers were separated and the aqueous layer extracted with three 200 ml portions of ether. The combined organic layers were dried over magnesium sulfate and the solvents removed in vacuo. The crude product was added to 500 ml of ice cold five percent hydrochloric acid and heated to 90° C over a 20 min period. The mixture was saturated with salt and the layers separated. The aqueous layer was saturated with salt and extracted with four 50 ml portions of ether. The combined organic layers were dried over magnesium sulfate and the solvents removed in vacuo. The crude mixture was dissolved in ca 150 ml of 95 percent ethanol, 0.5 g of five percent palladium on charcoal added and the mixture placed on a Parr shaker under 45 psi of hydrogen and shaken for two hours. The catalyst was removed by filtration and 23.0 g (0.0093 moles) of Girard's T Reagent added. The reaction mixture was refluxed for one hour and cooled to room temperature, then poured into a mixture of 250 ml each of ether and water. The layers were separated and the ether layer extracted with two 50 ml portions of water. Concentrated hydrochloric acid, 40 ml, was added to the combined water layers and the aqueous solution heated for 30 min on a steam bath. The mixture was cooled to room temperature and extracted with four 75 ml portions of ether. The combined ether layers were washed with two 50 ml portions

of saturated sodium bicarbonate solution and dried over magnesium sulfate. The solvents were removed in vacuo and the product distilled through a four inch Vigreux column to give 14.2 g (21 percent) of V, b.p. 90-91/19 mm Hg. (lit. 78-82°C/10 mm Hg (23)).

2,4,4-Trimethylcyclohex-2-en-1-one (VI)

A dried 250 ml three-necked round-bottom flask was fitted with a magnetic stirrer bar and dropping funnel and was placed under positive nitrogen flow. The pyrrolidine enamine of isobutraldehyde (24), 45.0 g (0.32 moles) was added to the flask and cooled to -5°C with an ice salt bath. Ethyl vinyl ketone (25), 31.0 g (0.36 moles) was added dropwise at a rate sufficiently slow to keep the reaction temperature below 2°C. The reaction was stirred for one hour at ice bath temperature after the addition was complete. A solution of 30 percent sulfuric acid, 300 ml, was added and the mixture stirred for 14 hrs at room temperature. The layers were separated and the aqueous layer extracted with three 50 ml portions of ether. The combined organic layers were washed with two 50 ml portions of saturated bicarbonate and dried over anhydrous magnesium sulfate. The solvents were removed in vacuo and the product distilled through a six inch Vigreux column yielding 36.2 g (82 percent) of VI, b.p. 73-74°C/17 mm Hg (lit 81-82°C/20 mm Hg) (26).

2,2,4-Trimethylcyclohexanone (VII)

Compound VII was prepared by catalytic hydrogenation of Compound VI. A solution of Compound VI, 15.0 g (0.108 moles) in ca 250 ml of 95 percent

ethanol was added to 0.5 g of 10 percent palladium on charcoal. The mixture was placed on a Parr shaker at 45 psi of hydrogen for 45 min. The catalyst was removed by filtration and the solvents removed in vacuo. Distillation through a four inch Vigreux column gave 14.2 g (93 percent) of VII, b.p. 74-75°C/21 mm Hg (lit. 87-89°C/30 mm) (26).

2,2,4,4-Tetramethylcyclohexanone (VIII)

Anhydrous liquid ammonia, ca 500 ml was distilled into a 1000 ml three-necked round-bottom flask fitted with a mechanical stirrer, and dry ice condenser and under positive nitrogen flow. Finely cut lithium wire, 0.36 g (0.051 moles) was added and the mixture stirred for 30 min. A solution of Compound VI, 2.76 g (0.02 moles) and anhydrous tert-butyl alcohol, 1.76 g (0.02 moles) in 50 ml anhydrous ether was added dropwise over 40 min. When the addition was complete, the mixture was stirred for 30 min, then 300 ml of anhydrous ether was added. A solution of 17.04 g (0.12 moles) of freshly distilled methyl iodide in 50 ml of anhydrous ether was added dropwise over 30 min. The reaction mixture was stirred for one hour. The dry ice condenser was replaced with an air condenser and the ammonia allowed to evaporate. Water, 200 ml, was added and the aqueous and organic layers were separated. The product was distilled through a four inch Vigreux column to give 1.60 g (46 percent) of VIII, b.p. 81-83°C/17 mm Hg.

Compound VIII had an ir absorption at 5.85 (C=O) and exhibited the following nmr spectrum: 2.2-2.5 (broad absorption, 2H), 1.5-1.85 (broad

absorption, 4H), 1.07 (s, 6H), 1.08 (s, 6H).

Anal. $C_{10}H_{18}O$

Calcd: C, 77.86; H, 11.75

Found: C, 77.62; H, 11.59

2-Methylcyclopentanone (IX)

This compound was prepared by a method similar to that of Bouveault (27). A mixture of 210 g (1.35 moles) of 2-carbethoxycyclopentanone and 240 g (1.69 moles) of methyl iodide was placed in a 2000 ml three-necked round-bottom flask fitted with a mechanical stirrer and dropping funnel. The flask was capped with a calcium chloride tube and the mixture was cooled with stirring to $-5^{\circ}C$. A solution of sodium ethoxide, prepared by dissolving 31.0 g (1.35 moles) of sodium metal in ca 800 ml of absolute ethanol was added dropwise at a rate sufficiently slow to keep the reaction temperature below zero degrees. When the addition was complete, the reaction mixture was allowed to warm to room temperature and stirred overnight. The solvents were removed in vacuo and the sodium iodide formed was removed by filtration. The crude methylation product was added to a solution of 80 g (1.43 moles) of potassium hydroxide in ca 800 ml of water and refluxed with stirring for 24 hrs. The reaction mixture was cooled, the layers separated and the aqueous layer extracted with three 100 ml portions of ether. The combined organic layers were dried over magnesium sulfate and the solvents removed in vacuo. Distillation at reduced pressure through a four inch Vigreux column gave 78.82 g (62 percent) of IX, b.p. $43-45^{\circ}C/18$ mm Hg (lit $136^{\circ}C/atm$) (27).

2, 5-Dimethylcyclopentanone (X)

A dried 1000 ml three-necked round-bottom flask fitted with a mechanical stirrer and dropping funnel was charged with 38.2 g (0.24 moles) of 2-carbethoxy-5-methylcyclopentanone (28) and 40.0 g (0.282 moles) of methyl iodide and cooled to -5°C with an ice salt bath. A solution of sodium ethoxide, prepared by dissolving 5.6 g (0.24 moles) of sodium metal in 80 ml of absolute ethanol was added dropwise at a rate sufficiently slow to maintain the reaction temperature at or below zero degrees C. When the addition was complete, the reaction mixture was stirred for one hour and the solvents were removed in vacuo. The sodium iodide formed in the alkylation was removed by filtration and the crude product added to 250 ml of five percent sodium hydroxide and refluxed for 70 hrs. The mixture was cooled to room temperature and the layers separated. The aqueous layer was saturated with salt and extracted with two 50 ml portions of ether. The combined organic layers were dried over anhydrous magnesium sulfate and distilled through a six inch Vigreux column giving 15.98 g (59 percent) of X, b. p. $141-43^{\circ}\text{C}$ (lit. $145-47^{\circ}\text{C}$)(29).

Phenyllithium

Phenyllithium was prepared by the method of Gilman (30). A dried 500 ml three-necked round-bottom flask was fitted with a mechanical stirrer dropping funnel and reflux condenser. Anhydrous ether, 100 ml, was charged into the flask and 7.29 g (1.05 moles) of finely cut lithium wire was added. A solution of 78.5 g (0.5 moles) of freshly distilled bromobenzene in 200 ml of anhydrous

ether was added dropwise at a rate sufficiently rapid to maintain the stirred reaction mixture at reflux temperature. After the addition was complete, the mixture was refluxed overnight. The mixture was filtered through glass wool to remove the lithium bromide formed and stored in a freezer.

General Procedure for Generation and

Acetic Anhydride Trapping of Lithium Enolates

A dried 500 ml three-necked round-bottom flask fitted with a mechanical stirrer, dropping funnel, reflux condenser, and a stopcock at the bottom was placed under positive nitrogen flow. A weighed amount of triphenylmethane was placed in the flask and freshly distilled anhydrous 1, 2-dimethoxyethane added. When the triphenylmethane had dissolved, an equivalent amount of an ether solution of phenyllithium was added and mixture stirred until a negative Gilman test for phenyllithium was achieved (31). The desired amount of the ketone being investigated was added. In the case of equilibrium enolates, the ketone was added dropwise neat. When generation of a kinetic enolate was desired, the ketone was added dropwise as a ca 10 percent solution in anhydrous 1,2-dimethoxyethane. Solutions of kinetic lithium enolates were stirred for one hour at room temperature prior to quenching. Equilibrium lithium enolate solutions were stirred for three hours at reflux, then overnight at room temperature prior to quenching.

The lithium enolate solutions were quenched by dropwise addition to a large excess (ca 10 fold) of acetic anhydride according to the procedure of

Ringold and Malnotra (32). The mixture was stirred for 30 min, then poured into a heterogeneous mixture of saturated sodium bicarbonate and hexane at 10°C. The mixture was stirred at 10°C and solid sodium bicarbonate added until evolution of carbon dioxide ceased. The solids were removed by filtration and the layers separated. The aqueous layer was extracted twice with ether and the combined organic layers dried over magnesium sulfate. Solvents were removed in vacuo and the resulting oils distilled through a short path head at reduced pressure.

General Procedure for Generation and

Acetic Anhydride Trapping of Potassium Enolates

A flask having a stopcock at the bottom such as that used in the generation of lithium enolates was fitted with a mechanical stirrer and dry ice condenser and placed under positive nitrogen flow. A known amount of triphenylmethane was placed in the flask and dissolved in a minimum amount anhydrous 1,2-dimethoxyethane (DME). Several milliliters of 1,3-butadiene were distilled into the flask and a quantity of finely cut potassium equivalent to the amount of triphenylmethane employed was added. The mixture was stirred for two hours and additional DME added to bring the tritylpotassium solution to the desired concentration. Ketone addition, quenching with acetic anhydride and workup were performed in a manner identical to that described for lithium enolates.

Kinetic Lithium Enolates of

2-Ethylcyclohexanone (III)

Using the general procedure previously described, a solution of 1.14 g (0.091 moles) of 2-ethylcyclohexanone was added to a solution of triphenylmethyl-lithium prepared from 4.88 g (0.02 moles) of triphenylmethane. Short path distillation gave 1.14 g (61) percent) b. p. $93-97^{\circ}\text{C}/19\text{ mm Hg}$ of a mixture of enol acetates of 2-ethylcyclohexanone. Product ratios as determined by nmr showed that the less substituted enol acetate predominated.

Less substituted enol acetate (XI) 94.4 percent

More substituted enol acetate (XII) 5.6 percent

A repeat of the above reaction and analysis of the product mixture by vpc (10 foot x 1/4 inch Dow 550 on firebrick column, 190°C) showed

Less substituted enol acetate XI 97.7 percent

More substituted enol acetate XII 1.3 percent

Average of two runs:

XI 96.1 percent

XII 3.9 percent

Compounds XI and XII were identified from their nmr spectra. Compound XI exhibited the following spectrum: δ 5.25 (m, 1H), 1.06-2.47 (broad absorption, 9H), 2.02 (s, 3H), 0.88 (t, 3H, $J=6.5\text{ Hz}$). The nmr spectrum of XII exhibited the following absorptions: δ 2.07 (s, 3H), 1.41 - 2.78 (broad absorption, 10H), 0.91 (t, 3H, $J=7.5\text{ cps}$). These spectra were determined on samples purified by preparative vpc on the above column.

<u>Anal.</u>	$C_{10}H_{16}O_2$	Calcd.	C, 71.39; H, 9.59
		Found	XI C, 71.48; H 9.70 XII C, 71.62; H 9.70

Equilibrium Lithium Enolates
of 2-Ethylcyclohexanone (III)

The general procedure previously described was employed. A solution of triphenylmethyllithium was prepared from 4.88 g (0.02 moles) of triphenylmethane and titrated to a clear endpoint with 2-ethylcyclohexanone. The ketone uptake was 1.93 g (0.0153 moles). A 25 percent excess (0.47 g) of 2-ethylcyclohexanone was added.

This mixture was processed in the usual manner to give a pale yellow oil which had b. p. 80-98°C/17 mm Hg and was a mixture of compounds III, XI and XII. The yield of enol acetates as determined by vpc using methyl benzoate as an internal standard was 31 percent. Analysis of the enol acetates by vpc showed:

XI, 20.3 percent

XII, 79.7 percent

The above reaction was repeated. Product ratios were

XI, 19.2 percent

XII, 80.8 percent

Average of two runs:

XI, 19.7 percent

XII, 80.3 percent

Kinetic Potassium Enolates
of 2-Ethylcyclohexanone (III)

The general procedure for the preparation of potassium enolate mixtures was employed. Triphenylmethylpotassium was prepared from 4.88 g (0.02 moles) of triphenylmethane and 0.78 g (0.02 moles) of potassium metal. A solution of 1.1 g (0.0087 moles) of 2-ethylcyclohexanone in ca 15 ml anhydrous DME was added dropwise. When the addition was complete, the reaction was stirred for one hour at room temperature, quenched and processed in the usual manner. Short path distillation gave 0.82 g (52 percent) of a mixture of enol acetates XI and XII, b. p. 94–100°C/19 mm Hg. Analysis of the mixture by vpc showed:

XI 66.7 percent

XII 33.3 percent

The above sequence was repeated and gave:

XI 67.9 percent

XII 32.1 percent

Average of two runs:

XI 67.3 percent

XII 32.7 percent

Equilibrium Potassium Enolates
of 2-Ethylcyclohexanone (III)

Triphenylmethylpotassium was prepared according to the general procedure, using 4.88 g (0.02 moles) of triphenylmethane and 0.78 g (0.02 moles) of potassium

metal. The solution was diluted with 60 ml of anhydrous DME. Titration of the solution with neat 2-ethylcyclohexanone required 1.80 g (0.143 moles) to reach a clear endpoint. A 25 percent excess (0.47 g) of the ketone was added. The mixture was processed according to the general procedure for equilibrium mixtures of potassium enolates. Short path distillation of the products gave 1.35 g of an oil, b. p. 89-97°C/17 mm Hg. Yield of enol acetates, as determined by vpc (10 foot Dow 550 column, 190°C) was 25 percent. Product ratios were also determined by vpc and gave

XI 48.3 percent

XII 51.7 percent

A repeat of the above sequence showed

XI 47.2 percent

XII 52.8 percent

Average of two runs

XI 47.8 percent

XII 52.2 percent

Alkylation of the Kinetic Lithium Enolates of
2-Ethylcyclohexanone (V) with Methyl Iodide

A dried 500 ml three-necked round-bottom flask was fitted with a mechanical stirrer and placed under positive nitrogen flow. Triphenylmethane, 4.88 g (0.02 moles) and 65 ml of anhydrous DME were added to the flask and stirred until the triphenylmethane dissolved. An equivalent amount of phenyllithium in

ether was added and the mixture was stirred for 30 min at which time a negative Gilman test for phenyllithium (31) was obtained. A solution of 1.38 g (0.011 moles) of V in 10 ml of anhydrous DME was added. The mixture was stirred for 45 min and 14.3 g (0.10 moles) of freshly distilled methyl iodide was added. The reaction mixture was stirred for 15 min and poured into 200 ml of water. The layers were separated, the aqueous layer extracted with three 50 ml portions of ether and the combined organic layers dried over magnesium sulfate. The solvents were removed in vacuo and the product was distilled through a short path head, to give 1.03 g of a clear oil b.p. 83–84°C/19 mm Hg. Analysis of the distillate by vpc (10 foot x 1/4 inch SE-30 on Diatoport 150°C) showed only one significant component, identified as 2-ethyl-6-methylcyclohexanone (XIII). Compound XIII exhibited the following nmr spectrum: δ 1.10–2.80 (broad absorption, 10H), 0.97 (d, 3H, J=8 Hz), 0.94 (t, 3H, J=6 Hz)

<u>Anal.</u>	$C_8H_{14}O$	Calcd	C, 77.08; H, 11.43
		Found	C, 77.24; H, 11.35

Kinetic Lithium Enolate of

2-Isopropylcyclohexanone (V)

The general procedure for generation and trapping of lithium enolates was employed. Triphenylmethyllithium was prepared from 4.88 g (0.02 moles) of triphenylmethane and 1.50 g (0.0107 moles) of 2-isopropylcyclohexanone added as a 10 percent solution in anhydrous DME. Short path distillation gave 1.05 g (57 percent) of a pale yellow oil b.p. 97–99°C/21 mm Hg. This oil showed only a single component by vpc (10 foot x 1/4 inch SE-30 on Diatoport column) and

was further purified by preparative vpc. The oil was identified from its nmr spectrum as the less substituted enol acetate of 2-isopropylcyclohexanone (XIV).

Compound XV exhibited the following spectral properties: δ 5.30 (m, 1H), 2.0 (s, 3H, 1.26 - 2.60 (broad absorption, 8H, 1.0 (d, 3H, J=6.5 Hz), 0.81 (d, 3H, J=6.5 Hz).

<u>Anal.</u>	$C_{11}H_{18}O_2$	Calcd	C, 73.03; H, 9.93
		Found	C, 72.76; H, 10.01;
			C, 72.79; H, 9.94

A repeat run of the above reaction gave compound XIV as the only enol acetate.

Equilibrium Lithium Enolates of

2-Isopropylcyclohexanone (V)

The general procedure for generation and trapping of a lithium enolate mixture was followed. Triphenylmethane 4.88 g (0.02 moles) was treated with an equivalent amount of phenyllithium in ether. 2-Isopropylcyclohexanone was added neat; 2.55 g (0.0183 moles) were required to reach a clear endpoint. Excess ketone, 0.63 g was added and the enolate mixture processed in the usual manner. Short path distillation of the product gave a 1.93 g of a light yellow oil, b.p. 79-98°C/19 mm Hg. The oil was analyzed and collected by vpc (10 foot x 1/4 inch SE-30 on Diatoport)

XIV 19.0 percent

XV 81.0 percent

Compound XVI was identified from its nmr spectrum: δ 2.02 (s, 3H), 1.33 - 2.32

(broad absorption 9H, 0.90 (d, 6H, J=7.0 Hz).

<u>Anal.</u>	$C_{11}H_{18}O_2$	Calcd	C, 73.03; H, 9.93
		Found	C, 72.77; H, 9.97

The yield, as determined by vpc on the aforementioned column using methyl benzoate as an internal standard, was 25 percent. A repeat of the above sequence of reactions gave

XIV 24.7

XV 75.3

Average of two runs

XIV 21.9

XV 78.1

Kinetic Potassium Enolates of

2-Isopropylcyclohexanone (V)

The general procedure for generation of potassium enolates was employed. Triphenylmethane, 4.88 g (0.02 moles) was dissolved in ca 15 ml of anhydrous DME. Approximately seven milliliters of butadiene was distilled into the flask and 0.78 g (0.02 moles) of finely cut potassium metal added. The mixture was stirred for 45 min, diluted with 60 ml of anhydrous DME, and 1.35 g (0.0096 moles) of compound VI in ca 15 ml of anhydrous DME was added dropwise. The enolate solution was stirred for one hour, quenched, and processed in the usual manner. Short path distillation gave 0.95 g (50 percent) of an enol acetate mixture b.p. 92-95°C/13 mm Hg. Analysis of this mixture by vpc (10 foot x 1/4 inch

SE-30 on Diatoport column, 190^oC) showed:

XIV 79.8 percent

XV, 20.2 percent

A repeat run of the above reaction showed

XIV 77.0 percent

XV 23.0 percent

Average of two runs:

XIV 78.9 percent

XV 21.1 percent

Equilibrium Potassium Enolates of

2-Isopropylcyclohexanone (V)

Triphenylmethylpotassium was prepared from 2.44 g (0.01 moles) of triphenylmethane using the general procedure previously described. After dilution with 30 ml of anhydrous DME, titration with neat 2-isopropylcyclohexanone required 0.5 g (0.00286 moles) of ketone to reach a clear endpoint. Excess 2-isopropylcyclohexanone, 0.12 g was added. The reaction mixture was stirred overnight and processed in the usual manner. Short path distillation of the products gave an oil b.p. 84-96^oC/16 mm Hg. Yield of enol acetates, as determined by vpc (10 foot x 1/4 inch SE-30 on Diatoport column, 200^o) using methyl benzoate as an internal standard, was 26 percent. Analysis of the mixture by vpc on the same column showed:

XIV, 34.5 percent

XV, 65.5 percent

A repeat run of the above reaction showed

XIV, 37.0 percent

XV, 61.0 percent

Average of two runs:

XIV, 36.7 percent

XV, 63.3 percent

Alkylation of the Kinetic Lithium Enolate of
2-Isopropylcyclohexanone (V) with Methyl Iodide

A dried 300 ml three-necked round-bottom flask was fitted with a mechanical stirrer and placed under positive nitrogen flow. Triphenylmethane, 4.88 g (0.02 moles) and 75 ml of anhydrous DME were added to the flask and an equivalent amount of ethereal phenyllithium added with a syringe. The mixture was stirred for 30 min at which time a negative Gilman test for phenyllithium was obtained (31). A solution of 1.24 g (0.089 moles) of 2-isopropylcyclohexanone in ca 20 ml of anhydrous DME was added dropwise. When the addition was complete, the mixture was stirred for one hour. Ten milliliters of freshly distilled methyl iodide was injected in one portion and the reaction mixture was stirred for 15 min. The mixture was poured into 100 ml of water, the layers were separated, and the aqueous layer was extracted with three 30 ml portions of ether. The combined organic layers were dried over magnesium sulfate and the solvents removed in vacuo. Short path distillation gave 0.81 g (60 percent) of a yellow oil b. p. 93-95°C/17 mm Hg. This oil was further purified by preparative

vpc (10 foot x 1/4 inch SE-30 on Diatoport, 175⁰C) and identified from its nmr spectrum as 2-isopropyl-6-methylcyclohexanone (XVI).

Compound XVI exhibited the following nmr spectrum: δ 1.32-2.75 (broad absorption, 9H), 0.96 (d, 3H, J=6.5 Hz), 0.91 (d, 3H, J=6.5 Hz), 0.88 (d, 3H, J=5.5 Hz).

<u>Anal.</u>	$C_{10}H_{18}O$	Calcd	C, 77.86; H, 11.75
		Found	C, 78.06; H, 11.64

Equilibrations of Enol Acetate Mixtures

Enol acetate mixtures were equilibrated by a modification of the method of House and co-workers (1, 2). A small sample (50 to 100 mg) of a mixture of enol acetates derived from a given compound was collected by preparative vpc and placed in a six millimeter glass tube sealed off at one end. A few crystals of *p*-toluenesulfonic acid, dried by azeotropic removal of water with benzene were added and the tubes sealed. The sealed tubes were heated in an oil bath at 100⁰ \pm 5⁰ C for 14 hours. Analysis of the mixtures was performed as previously described.

A mixture of XI and XII so treated showed:

XI, 2 percent

XII, 98 percent

A mixture of XIV and XV treated according to the above procedure was shown to consist only of XIV.

Apparent Kinetic Lithium Enolates of

2,4,4-Trimethylcyclohexanone (VII)

Triphenylmethyllithium was prepared according to the general procedure previously described using 4.88 g (0.02 moles) of triphenylmethane. A solution of 1.24 g (0.0089 moles) of 2,4,4-trimethylcyclohexanone in 15 ml of anhydrous DME was added dropwise. The reaction mixture was stirred for one hour after the addition and processed in the usual manner. Some solids were noted in the unquenched reaction mixture: the conditions were designated apparent kinetic control as suggested by House (2). The enol acetate mixture derived from 2,4,4-trimethylcyclohexanone was not separated on any of several vpc columns. Product ratios were determined from integration of the nmr spectrum of sample of the enol acetate mixture collected by preparative vpc (10 foot x 1/4 inch SE-30 on Diatoport, 170°C).

The less substituted enol acetate XVII exhibited the following nmr spectrum: δ 4.87 (m, 1H), 8.05 (s, 3H), 1.10-2.13 (broad absorption, 6H), 0.99 (s, 6H), 0.94 (d, 3H, $J=8.5$ Hz).

The more substituted enol acetate XVIII exhibited the following nmr spectrum: δ 2.06 (s, 3H), δ 1.22-2.30 (broad absorption, 6H), δ 1.45 (s, 3H), δ 0.95 (s, 6H).

These spectra were obtained on the enol acetate mixtures. Integration of the nmr spectrum of the above mixture showed:

XVII 92.5 percent

XVIII 7.5 percent

The yield enol acetate was 1.08 g (64 percent) b. p. 87-89°C/22 mm Hg.

A repeat run of the above reaction showed:

XVII 95.4 percent

XVIII, 4.6 percent

Average of two runs:

XVII, 93.9 percent

XVIII, 6.1 percent

Equilibrium Lithium Enolates of

2,4,4-Trimethylcyclohexanone (VII)

The general procedure for generation and trapping of lithium enolates was employed. Triphenylmethane, 2.44 g (0.01 moles) was used. Titration of neat Compound VII required 1.12 g (0.008 moles) to reach a clear endpoint. Excess ketone, 0.23 g was added and the mixture processed according to the standard procedure for mixtures of equilibrium lithium enolates.

Analysis of product ratio by nmr showed no absorption in the vinyl region of the spectrum indicating that only Compound XVIII was present. Because of the inherent limitations of the analytical method the approximate product ratios were designated.

XVII < 5 percent

XVIII >95 percent

This determination was verified by a repeat run of the above reaction.

Kinetic Potassium Enolates of

2, 4, 4-Trimethylcyclohexanone (VII)

Triphenylmethylpotassium was prepared according to the standard procedure previously described. Triphenylmethane, 2.44 g (0.01 moles) and 0.39 g (0.01 moles) of potassium metal was used. A solution of 0.77 g (0.0053 moles) of compound VII was added dropwise and the reaction mixture processed in the usual manner. Short path distillation of the products gave 0.62 g (63 percent) of an enol acetate mixture b.p. 84-86°C/19 mm Hg. Analysis of the mixture by nmr showed:

XVII, 64.5 percent

XVIII, 35.5 percent

A repeat run of the above reaction gave:

XVII, 61.4 percent

XVIII, 38.6 percent

Average of two runs:

XVII, 62.9 percent

XVIII, 37.1 percent

Equilibrium Potassium Enolates of

2, 4, 4-Trimethylcyclohexanone (VII)

The general procedure for the preparation and trapping of potassium enolates was employed using 2.44 g (0.01 moles) of triphenylmethane and 0.39 g (0.01 moles) of potassium metal. Titration of neat 2, 4, 4-trimethylcyclohexanone

required 1.12 g (0.008 moles) to reach a clear endpoint. A 25 percent excess of VII, 0.28 g, was added and the mixture processed in the usual manner. Short path distillation of the products gave an oil, b.p. 75-90°C/21 mm Hg. An aliquot of the enol acetate mixture was collected by preparative vpc (10 foot x 1/4 inch SE-30 on Diatoport, 150°C) and analyzed by nmr. Product ratios were

XVII, 86.3 percent

XVIII, 13.7 percent

A repeated run of the above reaction showed:

XVII, 84.3 percent

XVIII, 15.7 percent

Average of two runs:

XVII, 85.3 percent

XVIII, 14.7 percent

Alkylation of the Kinetic Lithium Enolates of

2, 4, 4-Trimethylcyclohexanone with Methyl Iodide

Triphenylmethyllithium was prepared from 4.88 g (0.02 moles) of triphenylmethane as described. A solution of 1.45 g (0.103 moles) of compound VII in 15 ml of anhydrous DME was added dropwise and the mixture was stirred for one hour. Eight milliliters of methyl iodide was added in one portion and the mixture was stirred for 15 min. The solution was poured into 100 ml of water, the layers were separated and the aqueous layer was extracted with three 30 ml portions of ether. Solvents were removed in vacuo and the products distilled through

a short path head to give 1.03 g (43 percent) of a clear oil that was identified as 2,4,4,6-tetramethylcyclohexanone (XIX) by comparison with an authentic sample. Compound XIX exhibited the following spectral properties: ir (CCl_4) $5.85\ \mu$ ($\text{C}=\text{O}$); nmr δ 1.42-2.25 (broad absorption, 6H), 1.27 (s, 3H), 0.97 (s, 3H), and 0.9 (d, 6H, $J=7.0$ Hz).

Alkylation of the Equilibrium Lithium Enolates of
2,4,4-Trimethylcyclohexanone (VII) with Methyl Iodide

The equilibrium lithium enolates of Compound VII were generated using 4.88 g (0.02 moles) of triphenylmethane as previously described. The mixture was quenched by addition of 10 ml of freshly distilled methyl iodide in one portion. The mixture was stirred for 15 min and poured into 100 ml of water. The layers were separated and the aqueous layer extracted with three 50 ml portions of ether. The combined organic layers were dried over magnesium sulfate and the solvents were removed in vacuo. The products were distilled through a short path head giving 1.23 g of a clear oil, b. p. $79-84^\circ\text{C}/21$ mm Hg. Only one monoalkylation product, identified as 2,2,4,4-tetramethylcyclohexanone (VIII) by comparison with an authentic sample, was present.

Kinetic Lithium Enolates of
2-Methylcyclopentanone (IX)

The general procedure for generation and trapping of lithium enolates was employed. Triphenylmethane, 9.96 g (0.04 moles) was used. Tetrahydrofuran (THF), freshly distilled from lithium aluminum hydride, was used as the

solvent. A solution of 1.92 g (0.0196 moles) of Compound IX in THF was added dropwise and the mixture processed in the usual manner. Short path distillation of the products gave an oil b.p. 54-58°C/31 mm Hg. An aliquot of this oil was separated and collected by preparative vpc (10 foot x 1/4 inch Dow 550 on Firebrick, 160°C) and had identical spectral properties with the two enol acetates reported by House and Trost (2). Product ratios, as determined by vpc analysis on the above column showed:

XX, less substituted enol acetate, 80.5 percent

XXI, more substituted enol acetate, 19.5 percent

A repeat of the above reaction showed:

XX, 74 percent

XXI, 26 percent

Average of two runs:

XX, 77.3 percent

XXI, 22.7 percent

Alkylation of the Kinetic Lithium Enolates of

2-Methylcyclopentanone with Methyl Iodide

Triphenylmethane, 7.47 g (0.03 moles) was placed in a dried, nitrogen swept 300 ml three-necked round-bottom flask equipped with a mechanical stirrer. Tetrahydrofuran, 100 ml, was added, followed by an ethereal solution of phenyllithium containing ca 0.03 moles of phenyllithium. The mixture was stirred for 30 min. 2-methyl-cyclopentanone, 2.08 g (0.0211 moles) was added dropwise

and the reaction mixture was stirred for 30 min. Ten milliliters of freshly distilled methyl iodide was added and the mixture stirred for 15 min and processed in the usual manner. Distillation of the products through a four inch Vigreux column gave 1.48 g of a clear oil, b. p. 49-51°C/22 mm Hg. Analysis of the mixture showed:

2,2 dimethylcyclopentanone (XXII),	27.5 percent
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2,5 dimethylcyclopentanone (X),	72.5 percent
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Compound X was identified by comparison with an authentic sample.

Compound XXII had been reported by Haller and Cornubert (33) and was identified from its nmr spectrum: δ 2.18 - 1.62 (broad absorption, 6H), 0.90 (s, 6H).

Repeated runs of the above reaction with enolate generation at -8°C and -78°C did not effect the product ratios within \pm 5 percent.

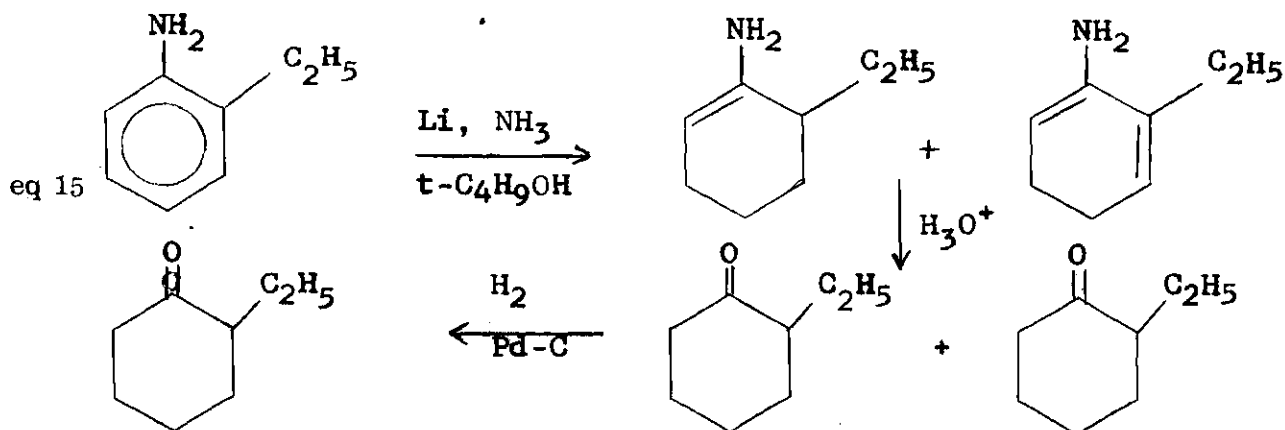
CHAPTER IV

DISCUSSION OF RESULTS

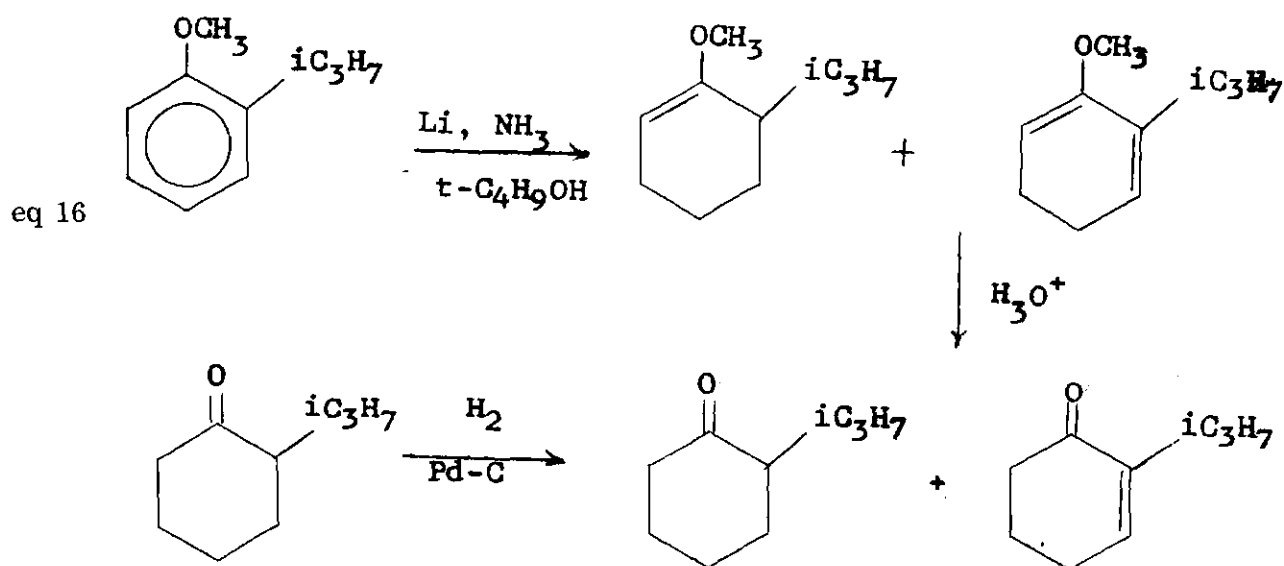
As indicated in Chapter I, this research consisted of three divisions. These divisions will be discussed in the sequence: synthesis of the starting ketones; generation and trapping of enolates mixtures and alkylation of lithium enolates.

The synthesis of 2-ethylcyclohexanone (III), 2-isopropylcyclohexanone (V), 2,4,4-trimethylcyclohexanone (VII) and 2-methylcyclopentanone (IX) were all accomplished by published procedures or modifications thereof.

2-Ethylcyclohexanone (III) was prepared by Birch reduction of o-ethyl-aniline according to the procedure of Stork and co-workers (20). The reduction, as shown in Equation 15 gives a mixture of enamines of 2-ethylcyclohexanone and 2-ethylcyclohex-2-en-1-one. The enamines were hydrolysed to the desired ketones under acidic conditions and the enone hydrogenated to the desired ketone.

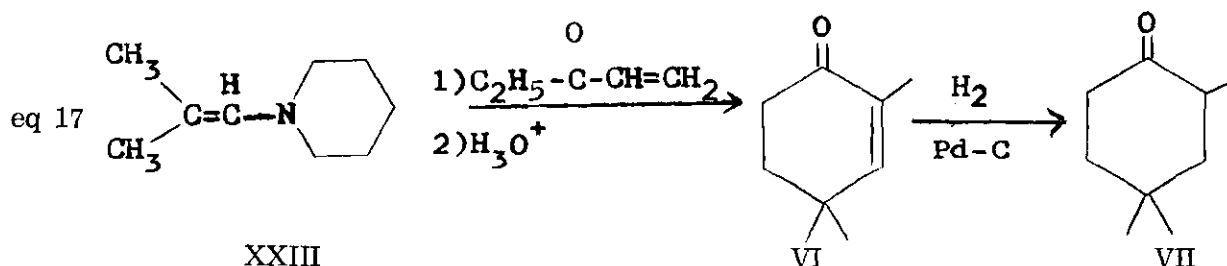


Compound V was prepared by Birch reduction of 0-isopropylanisole (IV), as described by Stork (20). The reduction gave a mixture of enol ethers, as shown in Equation 16. Acid hydrolysis of these enol ethers, followed by catalytic hydrogenation gave a mixture of the desired 2-isopropylcyclohexanone (V) and unreduced Compound IV. The mixture proved to be inseparable by fractional distillation but was separated cleanly by use of Girard's T Reagent.

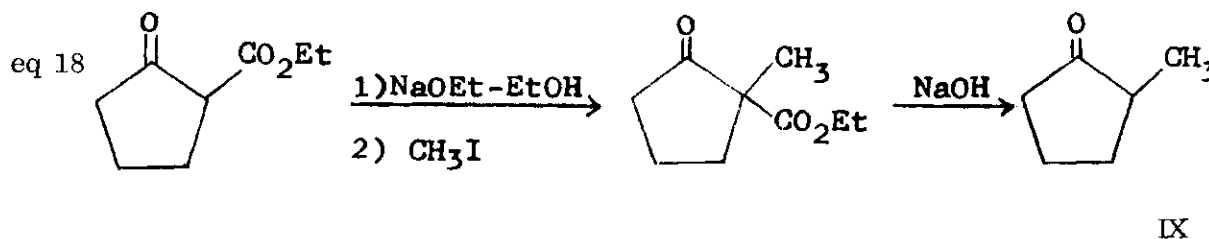


The preceding two examples, and the additional data of Stork (20) indicate that reduction of anilines is to be preferred over reduction of anisoles as a synthetic route to cyclohexanones. The reasons for preference of aniline reduction is that unreacted starting material can be washed away from the ketonic products with aqueous acid, while a more involved procedure is required to remove unreacted anisoles from their reduction products.

2,4,4-Trimethylcyclohexanone (VII) was prepared in a three step sequence from the pyrrolidine enamine of isobutraldehyde (24). Condensation of this enamine (XXIII) with ethyl vinyl ketone (25) followed by an acid catalysed cyclization gave 2,4,4-trimethylcyclohex-2-en-1-one (VI). Catalytic hydrogenation gave the desired compound VII as shown in Equation 17.

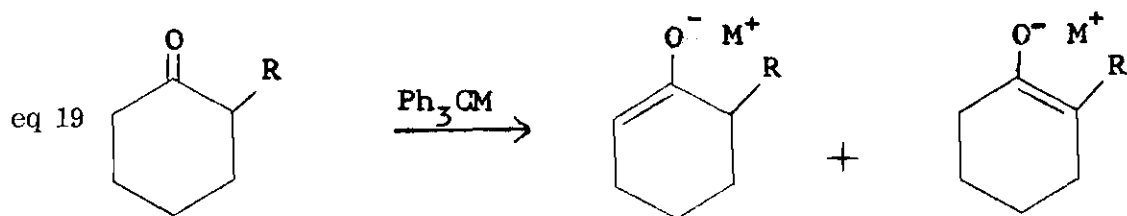


Compound IX, 2-methylcyclopentanone, was prepared by a modification of the method of Bouveault (27) as shown in Equation 18.



Methylation of 2-carbethoxycyclopentanone gave 2-methyl-2-carbethoxycyclopentanone. It was observed that on refluxing with aqueous sodium or potassium hydroxide, the methylated ketoester lost carbon dioxide to give the desired ketone (IX).

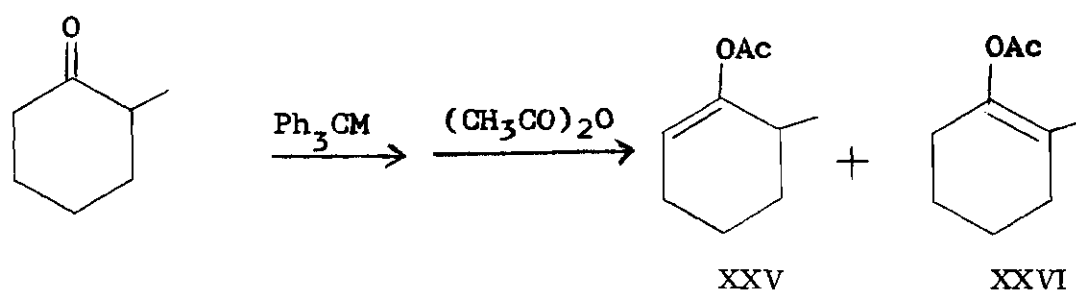
Ketones may be converted quantitatively to lithium and potassium enolates by triphenylmethyllithium and triphenylmethylpotassium respectively (2). When an unsymmetrically substituted ketone, such as a 2-alkylcyclohexanone is reacted with one of the above bases, two enolates can be generated, as shown in Equation 19.



It has been shown that enolate mixtures may be trapped with acetic anhydride to form relatively stable enol acetates (1, 19). By trapping enolate mixtures, it is possible to determine the ratio between the two enolates present.

Caine and Huff (33) and House and Kramar (1) have determined the composition of enolate mixtures derived from 2-methylcyclohexanone under several conditions. Results are given in Chart 2.

In Chart 2 and the following discussion, the term kinetic conditions is defined as a situation where excess triphenylmethyl carbanion is present. Kinetic enolate mixtures had a deep, blood red color characteristic of the triphenylmethyl carbanion. The term equilibrium conditions refers to a situation where the ketone



Metal	Conditions	XXV, percent	XXVI, percent	
Lithium	Kinetic	86	14	(33)
Lithium	Equilibrium	10	90	(33)
Potassium	Kinetic	70	30	(1)
Potassium	Equilibrium	<u>ca</u> 35	<u>ca</u> 65	(1)

Chart 2. Enolate Compositions of 2-Methylcyclohexanone in DME

being studied is in excess. Solutions of equilibrium enolates were clear and slightly yellow in color.

The steric effects on the position of enolization of 2-alkylcyclohexanones was studied by the generation and trapping of enolate mixtures derived from 2-ethyl-cyclohexanone (IV), 2-isopropylcyclohexanone (V) and 2,4,4-trimethylcyclohexanone (VII). The results are given in Chart 3.

Equilibration of the enol acetate mixtures with *p*-toluenesulfonic acid showed that the values given in Chart 3 are not those of equilibrated enol acetate mixtures.

The general trend indicated in Chart 3 is that as the steric bulk of the substituent at C-2 increases, proton removal at C-2 becomes less favorable with respect to proton removal at C-6. The conformation of a 2-alkylcyclohexanone with the alkyl group equatorial would be

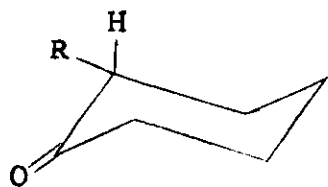


Figure 1

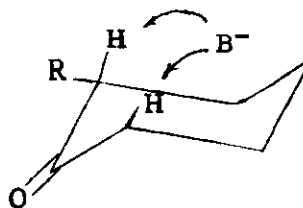
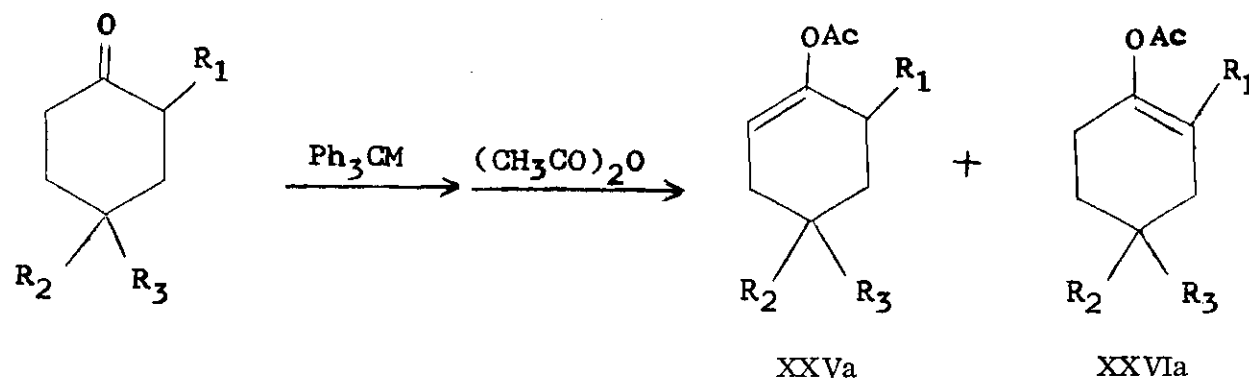


Figure 2

expected to be preferred (35). This conformation is shown in Figure 1. Axial proton removal, shown in Figure 2 is favored since removal of the axial proton gives a system in which there is continuous overlap of p-orbitals of the carbonyl group and the alpha carbon (36).

Since the base used in these studies is very bulky, interactions with the



R_1	R_2	R_3	Metal	Conditions	XXVa, percent	XXVIa, percent
C_2H_5	H	H	Lithium	Kinetic	97.3 ± 2	2.7 ± 2
C_2H_5	H	H	Lithium	Equilibrium	19.7 ± 1	80.3 ± 1
C_2H_5	H	H	Potassium	Kinetic	67.3 ± 2	32.7 ± 2
C_2H_5	H	H	Potassium	Equilibrium	47.8 ± 2	52.2 ± 2
$i\text{-C}_3\text{H}_7$	H	H	Lithium	Kinetic	100	0
$i\text{-C}_3\text{H}_7$	H	H	Lithium	Equilibrium	21.9 ± 3	78.1 ± 3
$i\text{-C}_3\text{H}_7$	H	H	Potassium	Kinetic	78.4 ± 3	21.6 ± 3
$i\text{-C}_3\text{H}_7$	H	H	Potassium	Equilibrium	36.7 ± 3	63.3 ± 3
CH_3	CH_3	CH_3	Lithium	Kinetic	93.9 ± 2	6.1 ± 2
CH_3	CH_3	CH_3	Lithium	Equilibrium	<5	> 95
CH_3	CH_3	CH_3	Potassium	Kinetic	62.9 ± 2	37.1 ± 2
CH_3	CH_3	CH_3	Potassium	Equilibrium	14.7 ± 1	85.3 ± 1

Chart 3. Enolization of Some 2-Alkylcyclohexanones

group at C-2 appear to force the base preferentially attack the axial proton at C-6. This phenomenon explains the increasing proton removal at C-6 as the bulk of the substituent at C-2 increases.

When the enolate mixtures were allowed to equilibrate, the general trend was to increasingly favor the more substituted enolate. Such an occurrence can be rationalized in terms of the generalization that the most substituted double bond is the most stable.

The observation that, in most cases, the lithium enolate shows a greater preference for one isomer than does the corresponding potassium enolate has been explained on the grounds that the lithium-oxygen bond is more covalent than the potassium oxygen bond. The increased covalency in the lithium case causes the double bond in the enolate anion to have more olefinic character (1).

The anomalous preference of the equilibrium potassium enolate for its more substituted isomer in the case of 2-isopropylcyclohexanone may be caused by interaction of the rather large potassium cation with the bulky isopropyl group. In the more substituted enolate, the substituent would be at its maximum possible distance from the oxygen atom.

In the case of 2,4,4-trimethylcyclohexanone, the axial methyl group at C-4 has a large effect on the position of enolization. This effect can be accommodated by invocation of steric interactions between the bulky base and the axial 4-methyl group. While these interactions would affect both the C-2 and C-6 sites, the proton at C-2 would be in a more hindered environment because of the presence of the C-2 methyl.

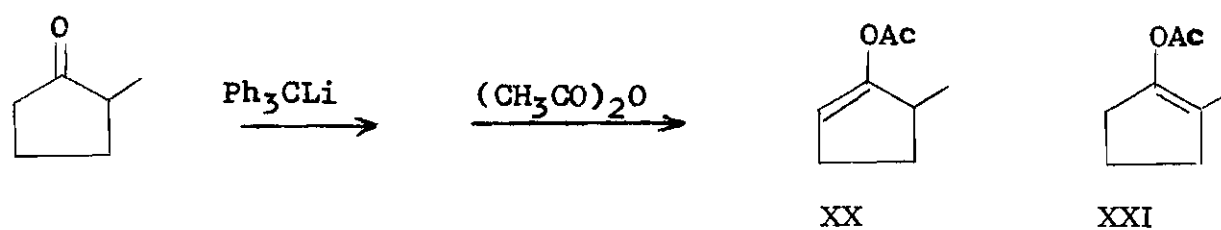
The kinetic lithium enolates of 2-methylcyclopentanone were studied in tetrahydrofuran (THF). Similar studies in DME were performed by House and Trost (19). Comparative results are given in Chart 4.

The slight difference in the results given in Chart 4 is likely due to the different solvents employed.

Enolization of 2-methylcyclopentanone was performed at lower temperatures: -8°C (ice salt bath) and -78°C (dry ice-acetone slurry). Tetrahydrofuran was employed as the solvent. It was hoped that by lowering the temperature, the percent of deprotonation at C-2 would be lowered. The enolate mixtures were trapped with methyl iodide. Results were comparable to enolizations performed at room temperature. Apparently energies of activation for proton removal are not sufficiently different for the temperature difference to be a factor in position of deprotonation.

The kinetic lithium enolates of all ketones studied and the equilibrium lithium enolates of 2,4,4-trimethylcyclohexanone were alkylated with methyl iodide. Results were similar to those obtained by trapping the same enolates with acetic anhydride, provided the methyl iodide was distilled immediately prior to use. Use of undistilled methyl iodide gave variable results. The products of these alkylations are tabulated in Chart 5.

As indicated in Chart 5, the alkylation of kinetic lithium enolates is a potentially useful synthetic route to 2,6-dialkylcyclohexanones, provided that the alkyl substituent present is large enough to cause proton removal to occur almost exclusively at C-6. When the above kinetic lithium enolates were alkylated

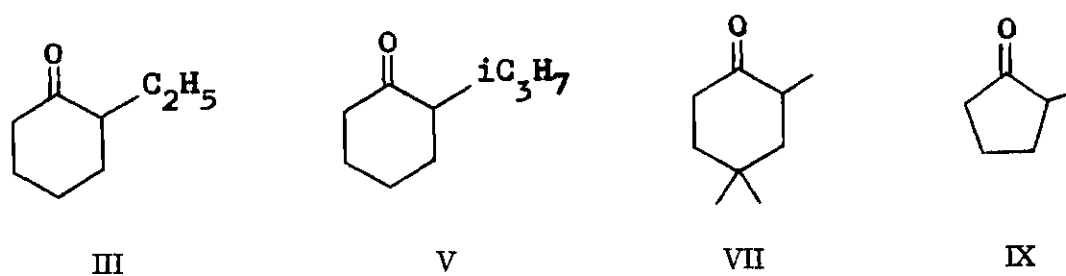


Solvent	XX, percent	XXI, percent
THF ^a	77.3 \pm 2	22.7 \pm 2
DME ^b	72	28

a) observed values

b) reference 2

Chart 4. Kinetic Lithium Enolates of 2-Methylcyclopentanone
in THF and DME



<u>Ketone</u>	<u>Conditions</u>	<u>2, 2 Dialkyl ketone, percent</u>	<u>2, 6 (or 2, 5) dialkyl ketone, percent</u>
III	Kinetic	0	100
V	Kinetic	0	100
VII	Kinetic	0	100
VII	Equilibrium	100	0
IX	Kinetic	27.5 ± 2	72.5 ± 2

Chart 5. Alkylation of Some Lithium Enolates with Methyl Iodide

with methyl iodide, no starting material was recovered. The alkylation of equilibrated lithium enolates suffers from the disadvantage that the excess starting ketone used to effect enolate equilibration must be separated from the alkylation products.

CHAPTER V

CONCLUSIONS

As the steric bulk of the alkyl substituent of a 2-alkylcyclohexanone increases, kinetically controlled proton removal at C-6 by triphenylmethyllithium becomes increasingly favored.

The presence of an axial 4-methyl group on a 2-alkylcyclohexanone likewise favors kinetically controlled proton removal at C-6 by triphenylmethyllithium.

The observation of Stork (15) that lithium enolates equilibrate slowly with respect to reaction with alkylating agents extends to the systems studied.

The potassium enolates derived from the ketones studied equilibrate much more rapidly than do the corresponding lithium enolates.

The alkylation of kinetic lithium enolates with methyl iodide represents a potentially useful route to 2-alkyl-6-methylcyclohexanones in cases where C-2 proton removal is sufficiently hindered.

Alkylation of equilibrium lithium enolates with methyl iodide suffers from the difficulty that an excess of starting ketone is used to effect the equilibration and must be separated from the methylated product. This cannot generally be accomplished by simple means.

CHAPTER VI

RECOMMENDATIONS

The effect of an alkyl group at the three positions, such as 3-methylcyclohexanone and menthone, which theoretically would hinder the protons at C-2, should be studied.

The study of a compound substituted so as to stabilize a negative charge at C-2, such as 2-phenylcyclohexanone should be studied, especially under kinetic conditions.

The use of other alkylating agents such that the alkylated product could be further reacted to form bicyclic systems, such as 1,3-dichloro-2-butene, should also be studied.

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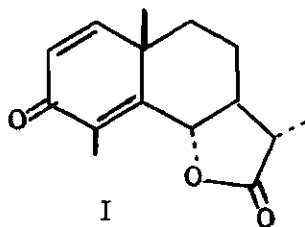
PART II

CHAPTER I

INTRODUCTION

Photochemical reactions of organic compounds have been sporadically reported in the literature since about 1900, with interest in these reactions greatly increasing during the past two decades. This interest is manifested in many research publications on organic photochemistry and in the appearance of several books and review articles (1-5). A few of the many organic photochemical reactions reported include photocycloadditions, photochemical reactions of small ring carbonyl compounds, photochemically induced cis-trans isomerization of olefins and photochemical dimerization of enones.

One class of organic photochemical reactions that is of special interest is the photochemical rearrangement of cross-conjugated cyclohexadienones. Cyclohexadienone photochemistry has its origins in work done on the sesquiterpene α -santonin (I) by the groups



of Jeger (6a) and Barton (6b).

In general, the bicyclic 6/6 fused cross conjugated cyclohexadienones yield tricyclic enones, referred to as "lumiproductions" when irradiated in inert

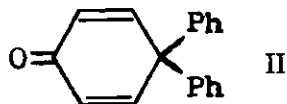
solvents such as p-dioxane or diethyl ether. On irradiation in protic media these same compounds have been observed to give fused 5/7 systems, spiro (4.5) systems, and phenols.

The exact mechanistic details of the photochemical reaction have not been determined, but it is possible to make some general statements concerning the reaction paths.

(1) The excited state intermediate is most probably a triplet. The triplet character of the intermediate is shown by the observation that triplet character and energy can be transferred from photosensitizers such as benzophenone to α -santonin (7). Further evidence for a triplet intermediate was obtained by irradiation of α -santonin at 3600 Å using piperylene (a triplet quencher) as a solvent. The reaction was completely quenched, ruling out a singlet intermediate, as the energy of the piperylene singlet (ca 2330 Å) is much higher than that of the applied radiation (7, 8).

(2) It is probable that the reactive species has n, π character, although π, π^* intermediates have not been completely ruled out. Cross-conjugated cyclohexadienones generally possess a strong absorption at ca 240 mμ ($\pi \rightarrow \pi^*$) and a weaker absorption at ca 300 mμ ($n \rightarrow \pi^*$). All rearrangements can be induced by radiation of either wavelength and since rearrangements occur at the longer wavelength (lower energy) $n \rightarrow \pi^*$ transition, it is thought that the reactive species has n, π^* character (9). Phosphorescence emission studies in a glass at low temperature by Fisch and Richards (7) gave a value of 68 ± 1 k-cal/mole, similar to the n, π^* triplet energy of benzophenone. Similarly, phosphorescence emission studies

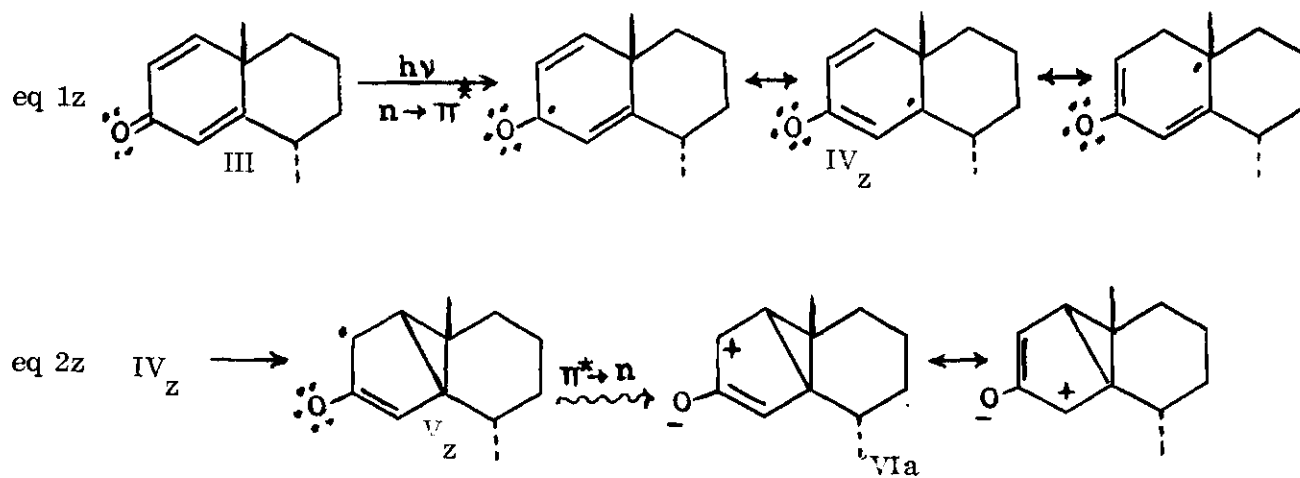
on the 4,4-diphenyl cross-conjugated cyclohexadienone (II)



by Zimmerman and Swenton (10) showed that the triplet energy was 68.8 k-cal/mole. This was assigned to n, π^* rather than higher energy π, π^* triplet based on analogy to the $n \rightarrow \pi^*$ and triplet energy of benzophenone, the short lifetime of the triplet (the π, π^* triplet would be expected to have a longer lived triplet than the 0.5 msec observed), and the characteristic $n \rightarrow \pi^*$ phosphorescence emission spectrum. Kropp has criticized these findings as favoring intermediacy of an n, π^* triplet over a π, π^* triplet because of the uncertainty of the relationship between the photochemical behavior of a molecule in a glass at 77°K and one in solution at room temperature (11).

The intermediacy of mesoionic species in the photochemical rearrangement of cross-conjugated cyclohexadienones is widely accepted. Several systems of notation for depicting the pathways by which these hypothetical zwitterions might arise have appeared in the literature (12, 13, 14). The notations suggested by Zimmerman and Schuster (12) and Taylor (14) are shown in Chart 1. While the Taylor notation appears to be a simpler depiction, Zimmerman has recently criticized it on the grounds that it fails to show the state of the promoted electron and also fails to give a more accurate description of the transformations involved (15). Compound III, studied by Kropp and Erman (16) is used for illustration in these charts as it yields all of the types of products on irradiation in protic media.

ZIMMERMAN NOTATION



TAYLOR NOTATION

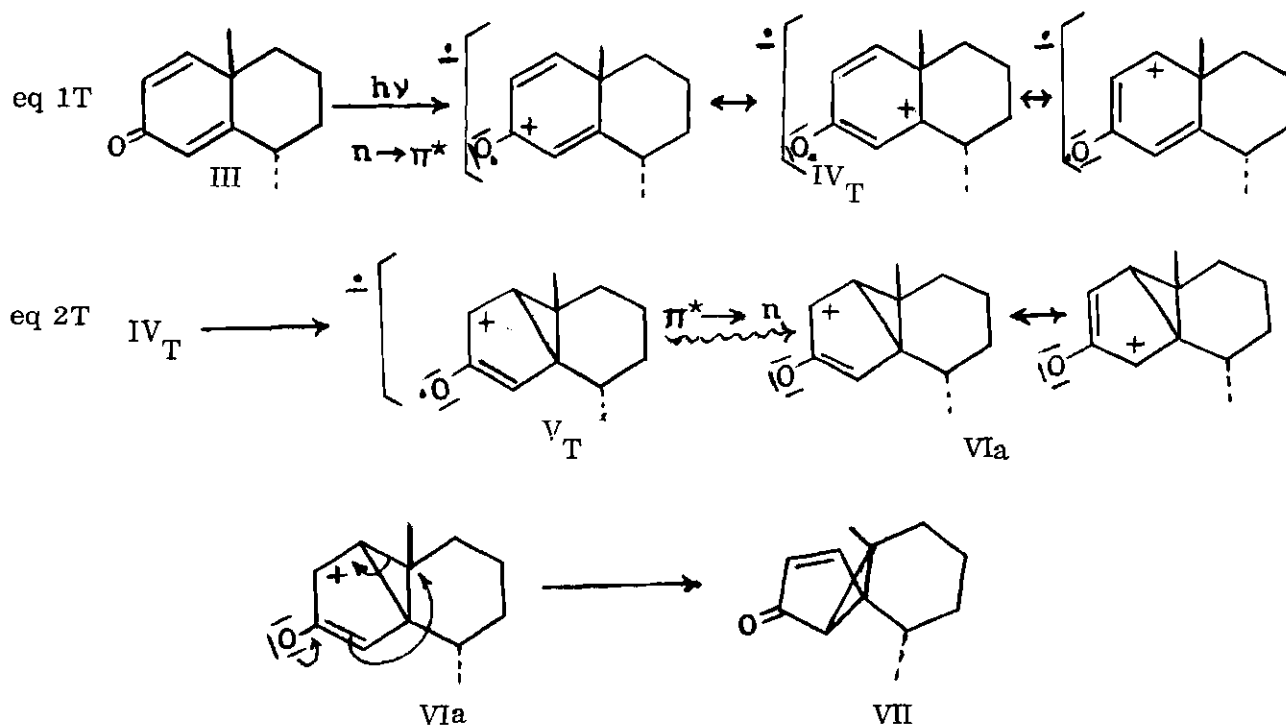
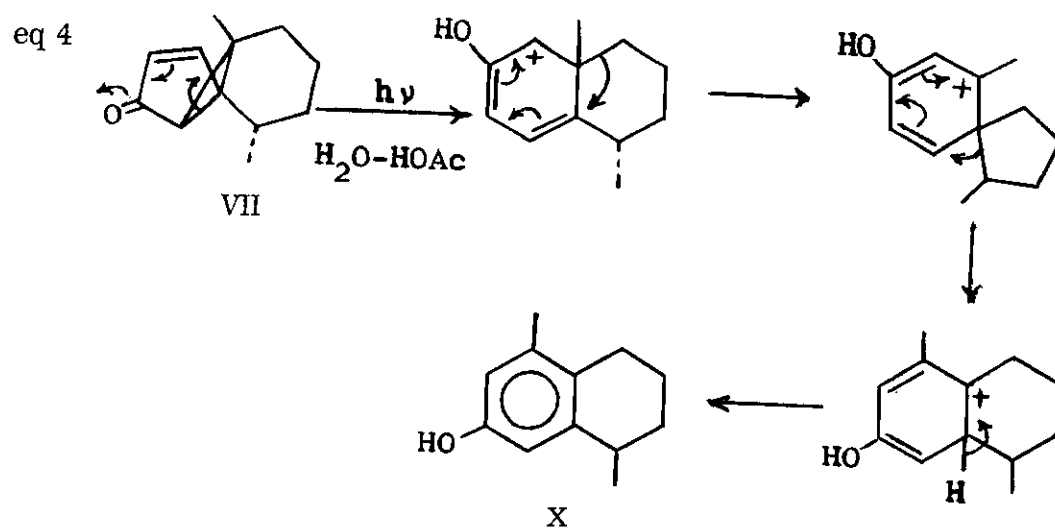
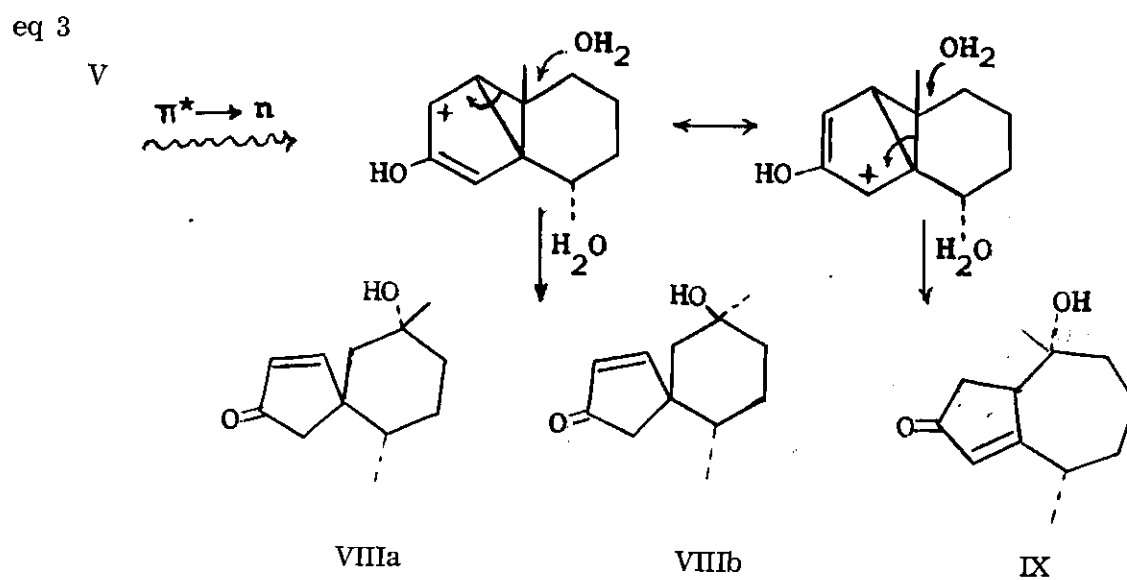


Chart 1. Mechanism of the Photochemical Rearrangement of
Cross-Conjugated Cyclohexadienones

Chart 1 (Concluded)



In the first step (Equation 1), III undergoes an $n \rightarrow \pi^*$ electronic transition to give the resonance stabilized triplet excited state IV. The species IV then rearranges to the excited state cyclopropyl intermediate V, as shown in Equation 2. The excited cyclopropyl species then undergoes a $\pi^* \rightarrow n$ transition. At this point, the character of the solvent is important. In an inert solvent such as dioxane, the $\pi^* \rightarrow n$ transition yields a zwitterionic hybrid, VIa (Equation 2) which can rearrange to the tricyclic ketone VII. In protic media, such as aqueous acetic acid (Equation 3), the electronic denotion yields the protonated form of the zwitterion, VIb. Solvent attack on VIb (Equation 3) at C₉ can lead to rupture of the C₁ - C₉ bond to give the epimeric spiro (4.5) hydroxyketones VIIa and VIIb or alternately to the 5/7 fused hydroxyketone IX via breaking of the C₉ - C₁₀ bond.

Phenol formation can be explained by further photochemical reaction of VII as shown in Equation 4. Kropp and Erman reported that on irradiation of III in aqueous acetic acid, VII was present after short reaction times, but was converted to X at the completion of the reaction.

An alternate possible mechanism that is not generally considered for rearrangements in aqueous acid solution is formation of the lumiproduet followed by nonphotochemical or "dark" reaction of this species with solvent to form non-phenolic products.

Many lumiproduets do, in fact, react with aqueous acid to give fused 5/7-hydroxyketones, spiro [4.5] hydroxyketones and dehydration products of these species. Three examples of this type of reaction are given in Chart 2 (17, 18).

The reason that this possibility is generally excluded is that these acid

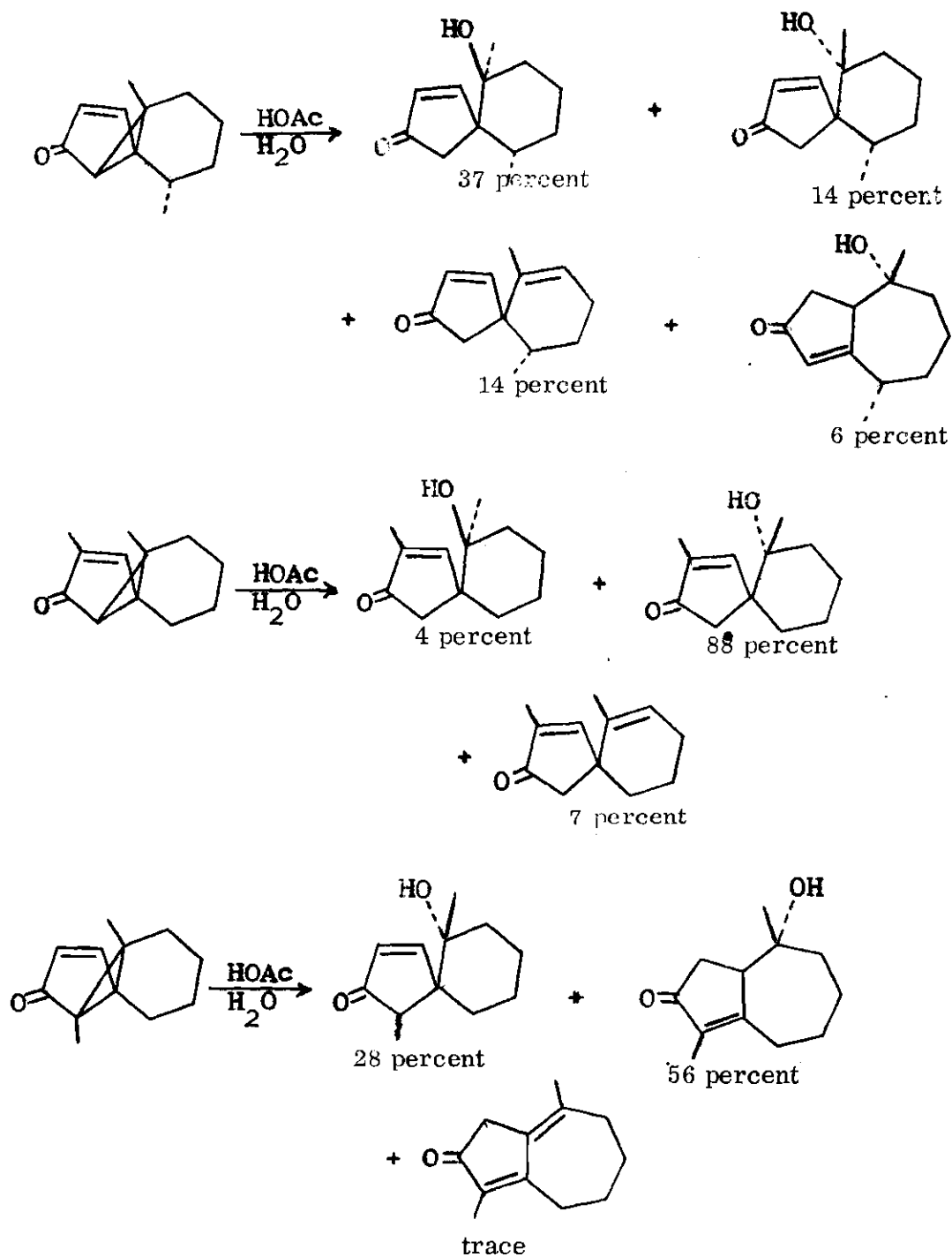


Chart 2. Acid Catalyzed Reactions of Lumiproducs

catalysed cleavages of lumiproductions usually require several hours at reflux, whereas most of the photochemical reactions reported were performed at 20 to 30°C. Additionally, the relative amounts of the various products formed are different in the acid catalyzed reactions of lumiproductions from those obtained in photochemical rearrangements of the cross-conjugated cyclohexadienones.

Equation (4) in Chart 1 represents a general, but not exclusive mode of photochemical reaction for lumiproductions in aqueous acidic media. Two examples of other types of photochemical rearrangements of lumiproductions in acidic media are shown in Chart 3 (17).

Equation 5 is an example of phenol formation not involving a spiro intermediate. Presumably the spiro intermediate X does not form because of the severe strain resulting from methyl-methyl interactions. Because of this strain, a 1,2 methyl shift is favored. (17)

The irradiation of lumisantoinin (eq 6) in aqueous acidic media also proceeds via a 1,2 methyl shift (6). The strain introduced by the trans fused lactone ring is said to prevent intermediacy of a spiro specie. Schuster and Fabian (19) reported that 6-epi- α -santonin rearranges via a spiro intermediate to a phenol and a new photoketone (eq 7) as well as by means of a 1,2-methyl shift to epimeric analogs of the products from α -santonin. The fact that this epimer allows formation of a spiro intermediate lends credence to the invocation of strain factors in explaining the rearrangement α -santonin via a 1,2-methyl shift.

Lumiproductions have also been shown to rearrange on extended irradiation in anhydrous dioxane. Lumisantoinin has long been known to rearrange to

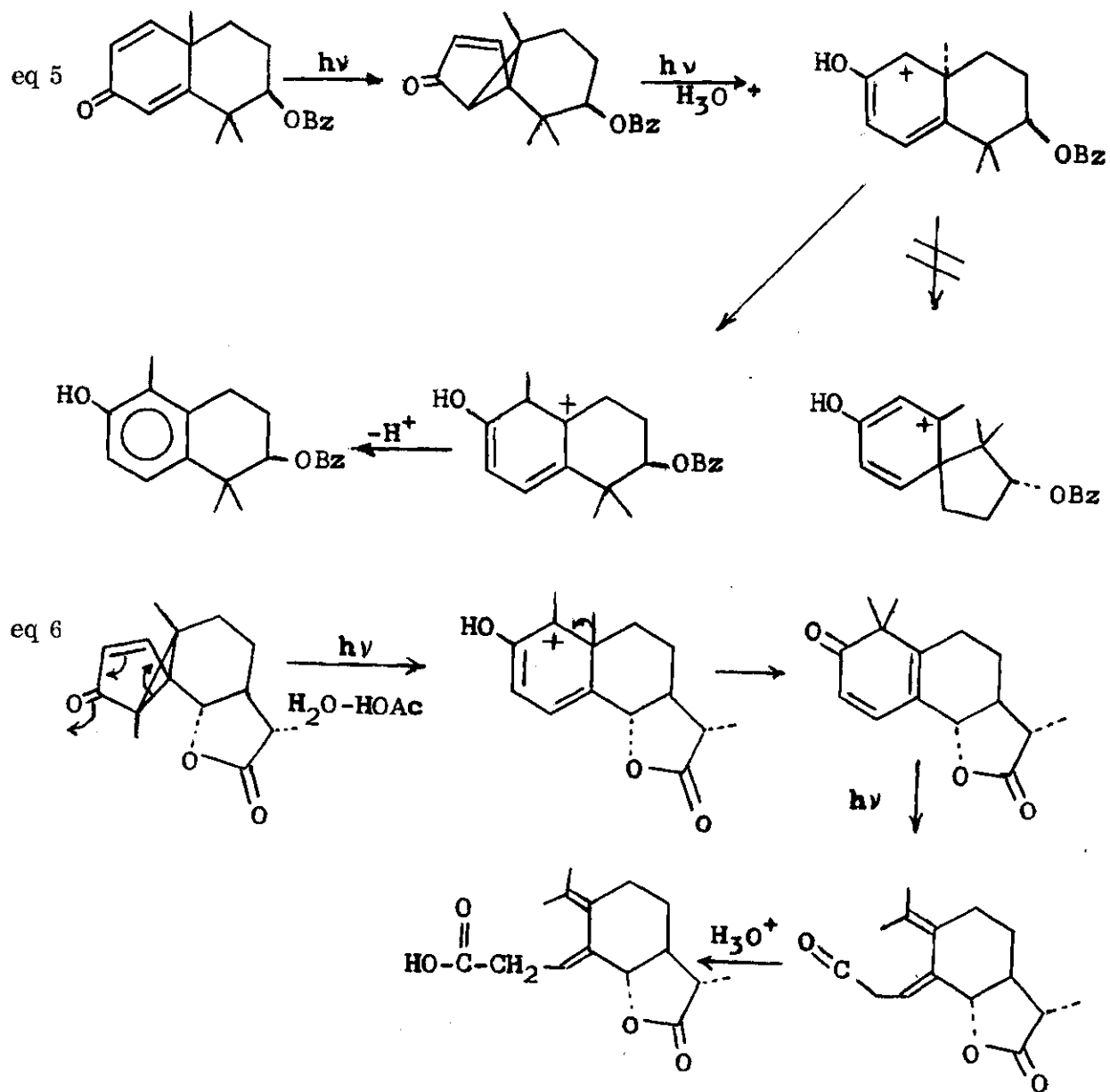
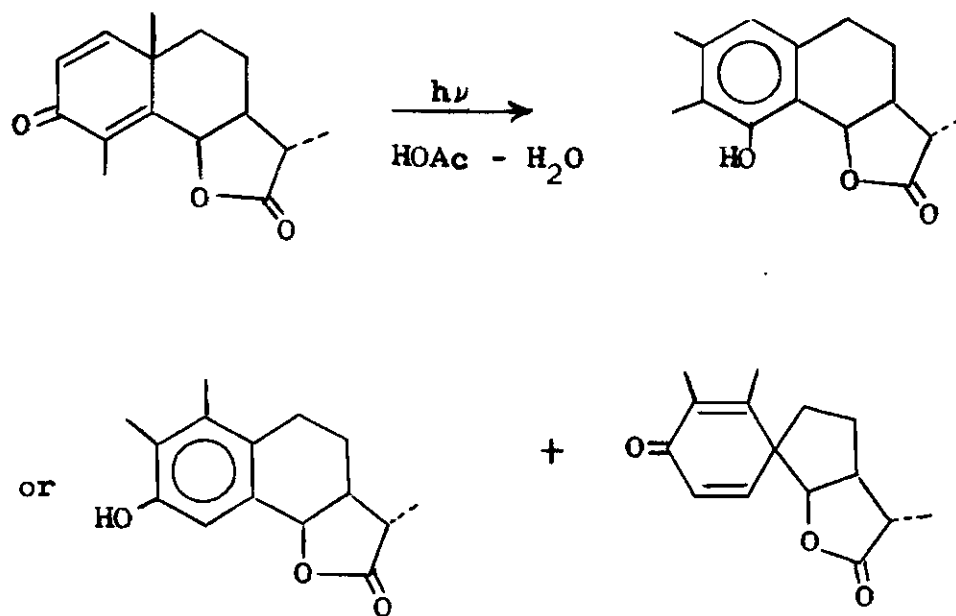


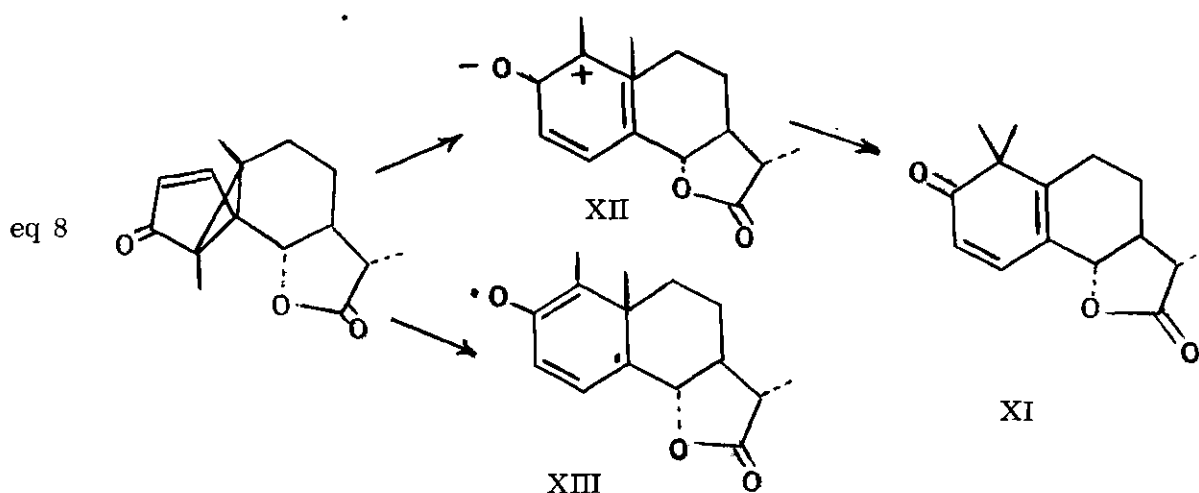
Chart 3. Anomalous Photochemical Reactions of Lumiproducs

Chart 3 (Concluded)

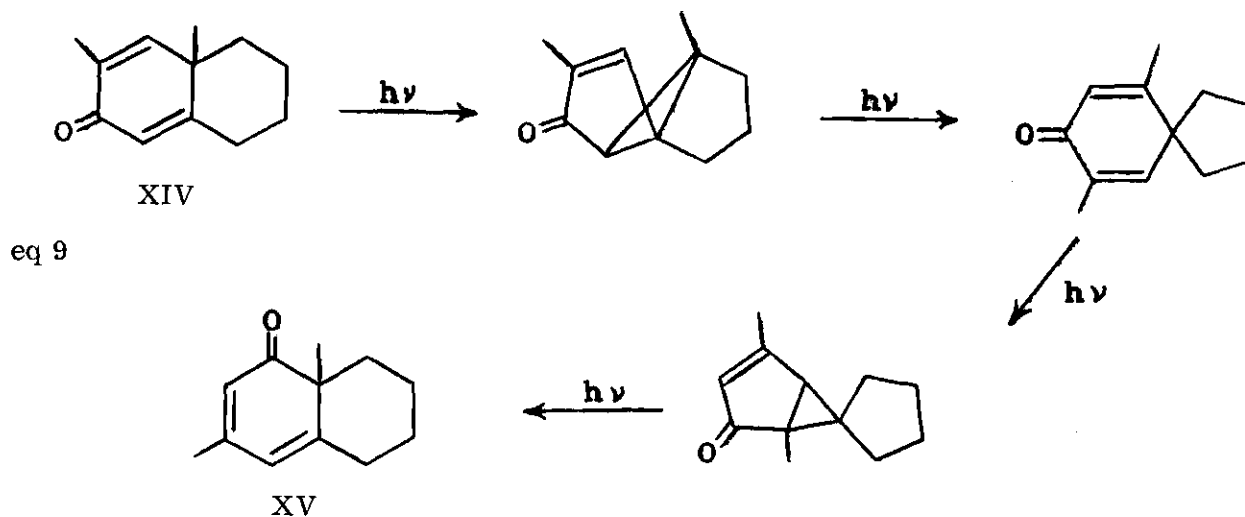
eq 7



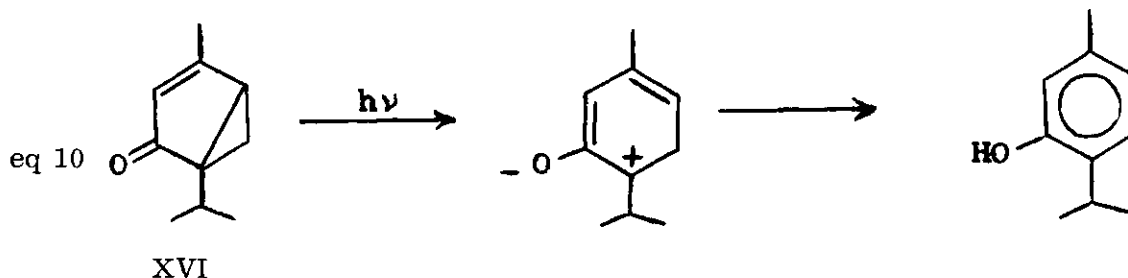
mazdasantonin (XI) on extended irradiation (6, 19). Fisch and Richards (20) recently reported that the intermediate in this reaction is the dipolar specie XII rather than the diradical XIII (eq 8). This finding is based on the observation that the blue intermediate trapped in a glass at low temperature had no paramagnetic character, as the diradical XIII would have.



The 2-methyl naphthalenone XIV rearranges to the linear dienone or "frozen phenol" XV on irradiation in dioxane (eq 9). (21)



Irradiation of neat samples of the monoterpene umbellulone (XVI), which is analogous to lumiproducs, has afforded quantitative conversion to thymol (eq 10) (22)



This is similar to irradiation in dioxane in that there is no external proton source as is present in aqueous acidic media.

The effect of methyl substitution at positions 2 and 4 on the photochemical rearrangements of bicyclic 6/6 fused cross-conjugated cyclohexadienones has been thoroughly studied. The effects of methyl substitution is summarized below.

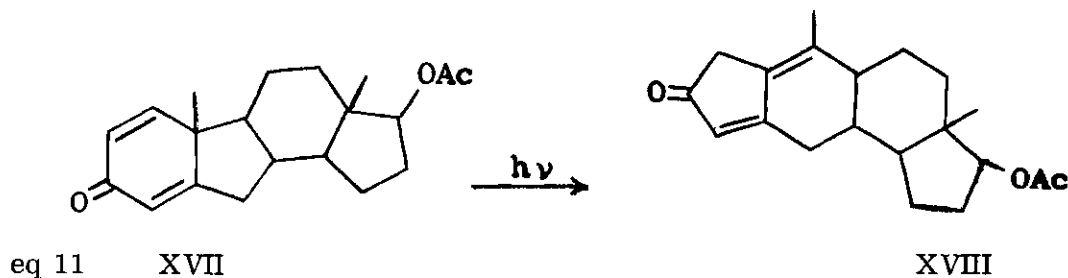
(1) Compounds with no methyl substitution on the A ring give lumiproducs in inert solvents and mixtures of spiro (4.5) hydroxyketones, 5/7 fused hydroxyketones and phenols in aqueous acetic acid.

(2) Compounds with a 2-methyl group give mainly lumiproducs in inert media and spiro hydroxyketones in aqueous acidic media.

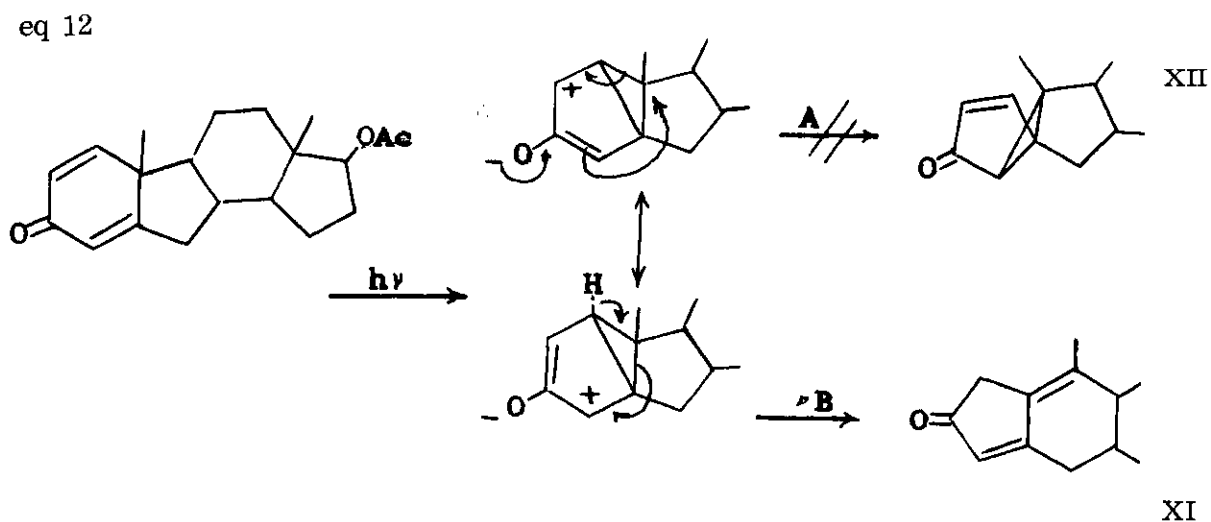
(3) Compounds with a methyl group at the four position give chiefly lumi-products in inert media and fused 5/7 - hydroxyketones in aqueous acidic media.

Only one example of a photochemical rearrangement of a cross-conjugated cyclohexadienone which is fused to a 5 membered ring has appeared in the literature. Jeger and co-workers (23) reported that on irradiation of the B-nor-steroidal dienone (XVII) in anhydrous dioxane at 2537 \AA , the linear conjugated dienone (XVIII)

forms in 68 percent yield (eq 11).

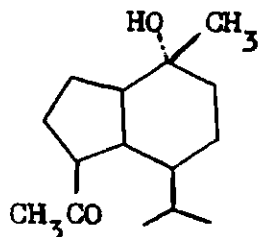


None of the expected tricyclic lumipproduct (XII) was formed. This phenomenon was attributed to excessive strain in the 5.3.5 tricyclic system. Jeger et al., postulated that the zwitterionic intermediate collapses with rupture of the 3a-7a bond to give XI (eq 13, Path B). Because of the strain thought to be inherent in the 5.3.5. ring system, the expected Path A is of much higher energy than Path B, and the lumipproduct (XII) is not formed.



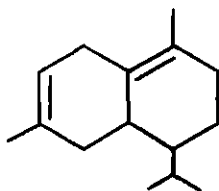
The purpose of this research was to investigate the photochemical behavior

of simpler 6/5 - fused bicyclic cross-conjugated cyclohexadienones in dioxane, including the effect of methyl groups at positions 4 and 6. Additionally, the photochemical behavior of these compounds was studied in aqueous acetic acid. The purpose of studying the behavior of these compounds was twofold: to compare their behavior with that of the corresponding 6/6 - fused systems and to investigate the feasibility of using a photochemical rearrangement of a 6/5 system in the synthesis of the sesquiterpene oplopanone (XX) (24).



XX

An additional possible application to natural product synthesis would be via ring expansion of the A-ring of the rearranged product as an entry into a series of compounds related to cadiene (XXI) (25).



XXI

CHAPTER II

INSTRUMENTATION AND EQUIPMENT

Melting points were determined on a Fisher Johns hot stage and are uncorrected. Carbon and hydrogen microanalyses were performed by Galbraith Laboratories, Incorporated, Knoxville, Tennessee. Ultraviolet spectra were recorded on a Cary Model 14 recording spectrophotometer using 1 cm balanced quartz cells with 95 percent ethanol as solvent. Infrared spectra were recorded on a Perkin Elmer Model 137 or Perkin Elmer Model 457 spectrophotometer. Proton magnetic resonance spectra were recorded on a Varian A-60 spectrometer using carbon tetrachloride (unless otherwise stated) as solvent. Positions of n. m. r. absorption are reported in ppm downfield from tetramethylsilane (TMS). The abbreviations s, d, t, q, and m refer respectively to singlet, doublet, triplet, quartet, and multiplet. Mass spectra were recorded on a Varian M-66 mass spectrometer. Solvents were removed with a commercial rotating evaporator unless otherwise stated. Vapor phase chromatography analyses and preparative vapor phase chromatography were performed on a Aerograph Model A-90P Manual Temperature Programmer Gas Chromatograph. Chromatography columns were prepared from commercial 80-200 mesh silica gel. Anhydrous magnesium sulfate was used as a drying agent in working up reactions.

All inorganic chemicals used in this research were reagent grade. Technical grade hydrocarbon solvents were used and were distilled prior to use.

Commercial anhydrous ether was stored over sodium metal ribbon and used without further purification. A Hanovia 450 watt high pressure mercury arc lamp, fitted with a Pyrex filter or used in an all Pyrex apparatus similar to that described by Kropp and Erman (16) was employed in all irradiation experiments where long wavelength light was desired. A Hanau 7 watt low pressure mercury arc lamp, which furnishes greater than ninety percent emission at 2537 \AA , was employed in other irradiation experiments. Solutions were deoxygenated prior to irradiation and agitated during irradiation with a stream of nitrogen.

CHAPTER III

EXPERIMENTAL

2-Methylcyclopentanone (XXII)

Compound XXII was prepared as described in Part I, Chapter III.

7, 7a-Dihydro-7a-methyl-5(6H)-indanone (XXIII)

Compound XXIII was prepared by a method similar to that reported by Ross and Levine (26). A dried 500 ml three-necked round-bottom flask equipped with a thermometer, dropping funnel, and magnetic stirring bar was placed under positive nitrogen flow. Anhydrous ether, 200 ml, was added to the flask and a solution of 2.8 g (0.05 moles) of potassium hydroxide in 20 ml of absolute ethanol was added. The mixture was cooled to -7°C with an ice-salt bath and 27.40 g (0.28 moles) of 2-methylcyclopentanone (XXII) was added. A solution of 9.0 g (0.129 moles) of methyl vinyl ketone in ca 50 ml anhydrous ether was added at a rate sufficiently slow to keep the reaction temperature at or below -5°C . When the addition was complete, the mixture was stirred for 45 min at -5°C , then for 45 min with the ice-bath removed. The mixture was poured into 200 ml of 10 percent hydrochloric acid and the layers were separated. The aqueous layer was saturated with salt and extracted with two 50 ml portions of ether. The combined organic layers were dried over magnesium sulfate and the solvents were removed in vacuo. Distillation at reduced pressure gave 7.1 g of 2-methylcyclopentanone (26 percent recovery) b.p. $41-42^{\circ}\text{C}/15\text{ mm Hg}$ and 14.04 of a tractable

mixture b.p. $68-105^{\circ}\text{C}/0.25\text{ mm Hg}$ which appeared, by infrared spectroscopy and vapor phase chromatography, to consist of XXIII plus its precursor diketone XXIV and ketol XXV. The tractable mixture was dissolved in 200 ml 10 percent ethanolic potassium hydroxide and refluxed in a nitrogen atmosphere for 30 min. The mixture was cooled to room temperature and neutralized with glacial acetic acid. The solvents were removed in vacuo, water was added to dissolve the potassium acetate formed in the neutralization, and the layers were separated. The aqueous layer was extracted with two 25 ml portions of ether and the combined organic layers were dried over magnesium sulfate. The solvents were removed in vacuo and the product was distilled at reduced pressure through a short path distilling head giving 10.9 g (57 percent) of XXIII b.p. $65-67^{\circ}\text{C}/0.30\text{ mm Hg}$ (lit. $112^{\circ}\text{C}/4\text{ mm Hg}$) (27).

Methyl Isopropenyl Ketone

This compound was prepared by the method of Morgan, Megson, and Pepper (28). Two hundred milliliters of 2-butanone and 150 ml of 40 percent aqueous formaldehyde were charged into a 1000 ml three-necked round-bottom flask fitted with a mechanical stirrer and reflux condenser. The flask was placed under positive nitrogen flow and 2 ml of 2 N sodium hydroxide solution was added. The mixture was stirred and heated on the steam bath until an exothermic reaction began; reflux continued for about two hours with no external heating. Occasional addition of 1 ml aliquots of 2 N sodium hydroxide was necessary to keep the mixture alkaline. The mixture was allowed to stir for 14 hrs and neutralized with glacial acetic acid. The reaction mixture was distilled through a six inch Vigreux

column.

<u>Boiling range</u>	<u>Pressure</u>	<u>Yield</u>
75-105°C	1 atm	<u>ca</u> 200 ml - discarded
88-110°C	15 mm Hg	57 g 3 hydroxy-methyl-2-butanone
110-140°C	15 mm Hg	<u>ca</u> 40 ml viscous oil-discarded

The crude 3-hydroxymethyl-2-butanone was dried with anhydrous sodium sulfate. Twenty grams of the crude hydroxyketone was treated with ca 200 mg of anhydrous oxalic acid and distilled through a four inch Vigreux column yielding 15.1 g of the water azeotrope of the desired vinyl ketone, b. p. 80-85°C/1 atm. The azeotropic mixture was dried with anhydrous sodium sulfate and distilled through a four inch Vigreux column prior to use; b. p. 97-98°C (lit 98.5°C) (28).

6,7a-Dimethyl-7,7a-dihydro-5(6H)-indanone (XXVI)

In a dried 500 ml three-necked round-bottom flask, fitted with a magnetic stirring bar, dropping funnel and thermometer and under positive nitrogen flow, 2.8 g (0.02 moles) of potassium hydroxide in 20 ml absolute ethanol was dissolved in ca 200 ml of anhydrous ether. The reaction mixture was cooled to -5°C with an ice-salt bath and 29.4 g (0.334 moles) 2-methylcyclopentanone (XXII) was added. Fourteen grams (0.167 moles) of methyl isopropenyl ketone in ca 50 ml anhydrous ether was added dropwise with stirring, while the reaction mixture temperature was maintained at -5°C, then for 45 min with the ice-bath removed. The mixture was poured into 200 ml 10 percent hydrochloric acid. The layers were separated

and the aqueous layer extracted with two 50 ml portions of ether. The combined organic layers were dried with magnesium sulfate and the solvents were removed in vacuo.

Short path distillation at reduced pressure gave 5.1 g recovered 2-methylcyclopentanone (17 percent) b.p. 41-43°C/15 mm Hg.

Further distillation gave 18.0 g tractable materials b.p. 72-95°C/0.07 mm Hg.

The tractable materials were dissolved in 200 ml 10 percent ethanolic potassium hydroxide and refluxed with stirring in a nitrogen atmosphere for 75 min. The mixture was cooled, neutralized with glacial acetic acid, and the solvents were removed in vacuo. Water was added to dissolve the potassium acetate formed, the layers were separated, and the aqueous layer was extracted with two 25 ml portions of ether. The combined organic layers were dried with magnesium sulfate. The solvents were removed in vacuo and the resulting yellow oil was distilled through a short path distilling head yielding 12.7 g (46.5 percent) of XXVI, b.p. 61°C/0.05 mm Hg. Compound XXVI exhibited the following spectral properties:

uv max 238 m μ (E 10,700); ir (CCl₄) 3.37, 3.41, 3.48, 5.97 (conjugated carbonyl) and 6.85 μ

nmr δ 5.65 (m, 1H), 1.25-2.87 (broad absorption, 9H), 1.19 (s, 3H), 1.07 (d, 3H, J=7.0 Hz); mass spectrum (70 eV) m/e 164 (M⁺)

Anal C₁₁H₁₆O

Calcd: C, 80.41; H, 9.86

Found: C, 80.20; H, 9.84

4, 7a-Dimethyl-7, 7a-dihydro-5(6H)-indanone (XXVII)

Compound XXVII was prepared by condensation of ethyl vinyl ketone with 2-methylcyclopentanone XXII, in a manner similar to that described for 7, 7a-dihydro-7a-methyl-5-(6H)-indanone(XXIII). A dried 1000 ml three-necked round-bottom flask equipped with a dropping funnel, magnetic stirrer bar, and thermometer was placed under positive nitrogen flow. Anhydrous ether, 400 ml, was added to the flask and a solution of 4.5 g (0.08 moles) of potassium hydroxide in 30 ml of absolute ethanol was added. The mixture was cooled, with stirring to -5°C by means of an ice-salt bath, and 52.0 g (0.53 moles) of 2-methylcyclopentanone was added. A solution of 20.5 g (0.244 moles) of ethyl vinyl ketone in ca 150 ml of anhydrous ether was added dropwise at a rate sufficiently slow to maintain the temperature of the reaction at or below -5°C , then stirred for an additional hour with the cooling bath removed. The mixture was poured into 300 ml of 10 percent hydrochloric acid, and the layers were separated. The aqueous layer was extracted with two 50 ml portions of ether, and the combined organic layers were dried with magnesium sulfate. The solvents were removed in vacuo and the compound was distilled through a short path head at reduced pressure. Compound XXII, 25.8 g (49 percent recovery) b. p. $43-44^{\circ}\text{C}/21\text{ mm Hg}$ was recovered, followed by 20.1 g of tractable material, boiling $99-113^{\circ}\text{C}/1.0\text{ mm Hg}$. The tractable material was dissolved in 300 ml 10 percent ethanolic potassium hydroxide and refluxed for 30 min in a nitrogen atmosphere. The mixture was cooled to room temperature, neutralized with glacial acetic acid, and the solvents were removed in vacuo. Water was added to dissolve the potassium acetate, the

layers were separated, and the aqueous layer was extracted with two 25 ml portions of ether. The combined organic layers were dried with magnesium sulfate and the solvents were removed in vacuo. Distillation of the resulting yellow oil through a short path head gave 12.7 g (33 percent) of XXVII, b. p. $87^{\circ}\text{C}/0.85\text{ mm Hg}$. Compound XXVII exhibited the following properties:

uv max $247\text{ m}\mu$ (ϵ 13,700); ir (CCl_4) 3.32, 5.99 (unsaturated $\text{C}=\text{O}$), 6.20 ($\text{C}=\text{C}$), $6.85\text{ }\mu$

nmr δ 1.7-2.91 (broad absorption, 10H), 1.59 (s, 3H), 1.13 (s, 3H)

Anal $\text{C}_{11}\text{H}_{16}\text{O}$

Calcd: C, 80.40; H 9.82

Found: C, 80.21; H 10.00

7a-Methyl-5(7aH)-indanone (XXVIII)

Compound XXVIII was prepared by the method of Bloom.(29) A dried 1000 ml three-necked round-bottom flask equipped with a reflux condenser and magnetic stirring bar was placed under positive nitrogen flow and 750 ml freshly distilled tert-butyl alcohol and seven milliliters glacial acetic acid was charged into the flask. Freshly sublimed selenium dioxide, 8.4 g (0.076 moles), was added and the mixture was stirred until the selenium dioxide dissolved. Compound XXIII, 11.3 g (0.075 moles), was added and the mixture was refluxed, with stirring, for 46 hrs. The mixture was concentrated to ca 200 ml by distillation of solvents in a nitrogen atmosphere. The selenium metal formed was removed by several filtrations, with suction, and the remaining solvents were removed in vacuo. The resulting black viscous mass was taken up in 250 ml of ether and filtered with suction. The ethereal solution was washed with five 50 ml portions of five percent

sodium hydroxide, dried with magnesium sulfate, and the solvents were removed in vacuo. Distillation through a short path head gave 2.3 g (21 percent) of XXVIII b. p. 70-71°C/0.3 mm Hg (lit 69-70°C/0.65 mm Hg) (29). The nmr spectrum of this compound had not been previously reported. It showed absorptions at δ 7.02 (d, 1H, $J_{AB} = 9.5$ Hz), 5.99 (d of d, 1H, $J_{AB} = 9.5$ Hz, $J_{BX} = 2.0$ Hz), 5.89 (m, 1H) 1.32-3.08 (broad absorption, 6H), 1.21 (s, 3H).

6,7a-Dimethyl-5(7aH)-indanone (XXIX)

Compound XXIX was prepared by a modification of the method of Bloom (29). A dried 100 ml three-necked round-bottom flask equipped with a reflux condenser and magnetic stirrer bar was placed under positive nitrogen flow. Seventy five milliliters of dried, freshly distilled tert-butyl alcohol was charged into the flask and 2.45 g (0.022 moles) of freshly sublimed selenium dioxide and 1 ml of glacial acetic acid were added. The mixture was stirred until the selenium dioxide dissolved and 3.28 g (0.02 moles) of XXVI was added. The mixture was refluxed with stirring for 30 hrs. The mixture was cooled to room temperature, and the selenium metal formed was removed by filtration with suction. The solvents were removed in vacuo leaving a viscous black mass that was distilled through a short path head to give 1.0 g of a brown oil b. p. 65-69°C/0.05 mm Hg. Analysis by vpc on a 10 foot x 1/4 inch column containing silicone SE-30 on chromosorb W showed that the oil consisted of ca 60 percent XXIX and 40 percent unreacted XXVI. The mixture was placed on a column of 25 g of silica gel. Elution with 300 ml of hexane and 450 ml of 5 percent ether-hexane gave recovered XXVI, mixed with a small amount of the desired compound XXIX. Further elution with

100 ml of five percent ether-hexane and 100 ml of ether gave 519 mg (16 percent) of XXIX. Compound XXIX exhibited the following spectral properties:

uv max 244 m μ (ϵ 12,900) ir (CCl₄) 3.36, 3.41, 3.45, 5.97 (conj C=O) and 6.14 (C=C) μ ; nmr; δ 6.72 (q, 1H, J=1.5 Hz), 5.88 (t, 1H, J=1.8 Hz), 1.41-2.92 (broad absorption, 6H), 1.79 (d, 3H, J=1.5Hz), 1.18 (s, 3H); mass spectrum (70 eV) m/e 162 (M⁺)

Anal C₁₁H₁₄O

Calcd: C, 81.44; H, 8.70

Found: C, 81.57; H, 8.91

4,7a-Dimethyl-5(7aH)-indanone (XXX)

Compound XXX was prepared by a modification of the method of Burn, Kirk and Petrow (30). A 1000 ml three-necked round-bottom flask equipped with a reflux condenser and magnetic stirrer bar was placed under positive nitrogen flow. Freshly distilled anhydrous p-dioxane, 500 ml, was charged into the flask and 9.35 g (0.0413 moles) of 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) was added. The mixture was stirred until the DDQ dissolved, and 6.60 g (0.0403 moles) of XXVII was added. The mixture was refluxed with stirring for 30 hrs. The solution was cooled to room temperature, and the solid 2,3-dichloro-5,6-dicyano-phydroquinone (DDHQ) was collected by filtration with suction. The mixture was concentrated to ca 50 ml by removal of solvents in vacuo. The mixture was cooled to room temperature and filtered with suction to remove the remaining DDHQ. It was then poured onto a loosely packed column of 70 g of alumina and eluted under pressure with 500 ml of benzene. The solvents were removed in vacuo and the resulting yellow oil was distilled through a short path head to give

3.92 g (60 percent) of XXX b. p. $88^{\circ}\text{C}/0.5\text{ mm Hg}$. Compound XXX exhibited the following spectral properties:

uv max $243\text{ m}\mu$ (E 11,900); ir 3.32, 6.01 (conj C=O), 6.21 (C=C) and 6.85μ

nmr; δ 6.99 (d, 1H, $J=9.5\text{ Hz}$), 6.02 (d, 1H, $J=9.5\text{ Hz}$), 1.15-2.83 (broad absorption, 6H), 1.72 (s, 3H), 1.17 (s, 3H)

Anal $\text{C}_{11}\text{H}_{14}\text{O}$

Calcd: C, 81.44; H, 8.70

Found: C, 81.29; H 8.66

Dehydrogenation of XXIII with DDQ

DDQ, 6.25g (0.0276 moles), was dissolved in ca 250 ml of anhydrous dioxane and placed in a 500 ml three-necked round-bottom flask which was equipped with a magnetic stirrer bar and reflux condenser. The apparatus was placed under positive nitrogen flow and 3.75 g (0.0254 moles) of compound XXIII was added. The mixture was fluxed with stirring for 23 hrs. The reaction mixture was cooled to room temperature, and the DDHQ formed was removed by filtration, with suction. The mixture was concentrated to a volume of ca 30 ml, placed on a loosely packed alumina column, and eluted under pressure with ca 500 ml of benzene. The solvents were removed in vacuo, and the resulting oil was distilled through a short path head to give 870 mg (24 percent) of a dienone mixture. This mixture appeared by uv analysis to consist of the desired cross-conjugated dienone XXVIII and the linearly conjugated dienone XXXI.

Dehydrogenation of XXVI with DDQ

A solution of 7.50 g (0.033 moles) of DDQ in ca 250 ml of anhydrous benzene was prepared and placed in a 500 ml three-necked round-bottom flask fitted with a magnetic stirrer bar and reflux condenser. The apparatus was placed under positive nitrogen flow and 4.92 g (0.03 moles) of compound XXVI was added. The mixture was refluxed with stirring for 23 hrs. The solution was cooled to room temperature, and the DDHQ was removed by filtration. The solution was concentrated in vacuo to ca 25 ml, placed on a loosely packed column of 75 g of alumina, and eluted under pressure with 500 ml of benzene. The solvents were removed in vacuo and the resulting oil was distilled through a short path head to give 900 mg of a mixture of dienones which appeared by nmr to be a mixture of the desired cross-conjugated dienone XXIX and its linearly conjugated isomer XXXII.

Irradiation of 7a-Methyl-5(7aH)-indanone (XXVII)

in Anhydrous Dioxane at 2537 Å⁰

Compound XXVII, 530 mg (0.0036 moles), was dissolved in ca 300 ml of anhydrous dioxane and irradiated with a Hanau seven watt low pressure mercury arc source. The reaction was monitored by vapor phase chromatography using a 10 foot SE-30 column; conversion to what appeared by vpc to be a single photoproduct was complete in 75 min. In a repeat reaction the yield of the photoproduct was 70 percent as determined by vpc using mesitylene as an internal standard. The solvents were removed in vacuo, and the crude oil was placed on a column of 12 g of silica gel. Elution with 200 ml of hexane gave 37 mg of a viscous

material that appeared to be polymeric and was discarded. Further elution with 550 ml of five percent ether-hexane gave 72 mg (13.6 percent) of a pale yellow oil which appeared by vpc to consist of greater than 90 percent pure 7a-methyl-3a,7a-dihydro-3a,7-cyclo-6(7H)-indanone (XXXIII). This was further purified by preparative vpc. Compound XXXIII exhibited the following spectral properties:

uv max 2.36 m μ (ϵ 6,300) and 271 m μ ; (ϵ 4,200) ir(CC1₄) 3.36, 3.38, 3.48 and 5.86 (conj C=O) μ

nmr; δ 7.28 (d, 1H, J=5.5 Hz), 5.77 (d of d, 1H, J_{AB}=5.5 Hz, J_{BX}=0.8 Hz), 1.47-2.27 (broad absorption, 7H), 1.66 (s, 3H); mass spectrum (70 eV) m/e 148 (M⁺)

Anal C₁₀H₁₂⁰

Calcd: C, 81.04; H, 8.16

Found: C, 80.99; H, 8.23

Further elution with ether-hexane mixtures and finally with pure ether gave what appeared by vpc to be a mixture of recovered starting material (XXVIII) and a new compound, an oil, identified as 7-methyl-5,6-dihydro-2(4H)-indenone (XXXIV). Compound XXXIV exhibited the following spectral properties:

uv max 296 m μ (ϵ 19,000); ir (CC1₄) 3.39, 3.41, 5.86 (conj C=O) 5.97 (C=C) and 6.31 (C=C μ); nmr δ 5.61 (s, 1H), 2.70 (s, 2H), 1.53 - 2.90 (broad absorption, 6H), 1.81 (s, 3H); mass spectrum (70 eV) m/e 148 (M⁺)

Anal C₁₀H₁₂⁰

Calcd: C, 81.04; H, 8.16

Found: C, 80.71; H, 8.47

Attempted Reaction of 7a-Methyl-3a, 7a-dihydro-
3a, 7-cyclo-6(7H)-indanone (XXXIII) with Silica Gel

Compound XXXIII, 30 mg (0.0002 moles) was placed on a column of 1.0 g of silica gel and a solution of five percent ether-hexane added to fill the column. The column was allowed to stand for ca 15 hrs, and the ether-hexane solution was eluted. Two hundred milliliters of ether was eluted through the column, and the solvents were removed in vacuo to give 28.5 mg of an oil which was shown to consist only of compound XXXIII by vpc analysis (10 foot x 1/4 inch SE-30 on Diatoport column, 190^oC).

Attempted Thermal Rearrangement of 7a-Methyl-
3a, 7a-dihydro-3a, 7-cyclo-6(7H)-indanone (XXXIII)

A small sample (25 to 50 mg) of compound XXXIII was sealed in a glass tube and heated at 100^oC for one hour. No change could be detected by vpc (10 foot x 1/4 inch SE-30 on Diatoport column, 190^oC).

Irradiation of 7a-Methyl-3a, 7a-dihydro-3a, 7-cyclo-6(7H)-
indanone (XXXIII) in Anhydrous Dioxane: Broad Spectrum Lamp

Compound XXXIII, 249 mg (0.00168 moles), was dissolved in ca 250 ml of anhydrous dioxane and irradiated for ten minutes with a 450 watt high pressure mercury arc source. The solvents were removed in vacuo, and the oily residue was placed on a silica gel column. Elution with hexane-ether mixtures gave no identifiable products.

Irradiation of 7a-Methyl-5(7aH)-indanone (XXVIII)

in Anhydrous Dioxane: Broad Spectrum Lamp

Compound XXVIII, 599 mg (0.00404 moles), was dissolved in ca 250 ml of anhydrous dioxane and irradiated for 90 min with a 450 watt high pressure mercury arc source. The solvents were removed in vacuo. The remaining resinous amber oil was placed on a silica gel column and eluted with hexane-ether mixtures. No identifiable products were isolated.

Irradiation of 6, 7a-Dimethyl-5(7aH)-indanone

(XXIX) in Anhydrous Dioxane

Compound XXIX, 427 mg (0.0026 moles), was dissolved in ca 250 ml of freshly distilled anhydrous dioxane and irradiated with a Hanau seven watt low pressure mercury arc source. The reaction was monitored by vapor phase chromatography; starting material was converted to a single photoproduct after 90 min irradiation. The solvents were removed in vacuo, and the crude oily product was placed on a column of eight grams of silica gel. Elution with 275 ml of hexane and 250 ml of 25 percent ether-hexane gave 286 mg (67 percent) of 5, 7a-dimethyl-3a, 7a-dihydro-3a, 7-cyclo-6(7H)-indanone (XXXV). Compound XXXV was further purified by preparative vpc and had the following properties:

uv max 235 m μ (ϵ 4, 630) and 283 m μ (ϵ 2, 120); ir (CCl₄) 3.33, 5.86 (conj C=O) μ ;

nmr δ 6.84 (m, 1H), 1.45 - 2.33 (broad absorption, 7H), 1.66 (d, 3H, J=1.5 Hz), 1.11 (s, 3H); mass spectrum (70 eV) m/e 162 (M⁺)

Anal $C_{11}H_{14}O$

Calcd: C, 81.44; H, 8.70

Found: C, 81.16; H, 8.90

Further elution with 150 ml of ether gave a small amount of resinous material which appeared to be polymeric and was discarded.

Irradiation of 4,7a-Dimethyl-5(7aH)-
indanone (XXX) in Anhydrous Dioxane

Compound XXX, 750 mg (0.0046 moles), was dissolved in ca 400 ml of anhydrous dioxane and irradiated for 120 min (48 percent conversion by vpc analysis). The solvents were removed in vacuo, and the crude oily photoproduct was placed on a column of 15 g of silica gel. Elution with 900 ml of hexane gave 276 mg (38 percent) of 1,7a-dimethyl-3a,7a-dihydro-3a,7-cyclo-6(7H)-indanone (XXXVI). Compound XXXVI exhibited the following spectral properties:

uv max 247 $m\mu$ (ϵ 4,820) and 274 $m\mu$ (ϵ 2,900); ir ($CHCl_3$) 3.30, 5.88 and 6.36 μ

nmr δ 7.28 (d, 1H, $J=5.5$ Hz), 5.74 (d, 1H, $J=5.5$ Hz) 1.56 - 2.80 (broad absorption, 6H), 1.18 (s, 3H) and 1.08 (s, 3H); mass spectrum (70 eV) m/e 162 (M^+)

Anal $C_{11}H_{14}O$

Calcd: C, 81.44; H, 8.70

Found: C, 81.24; H, 8.40

Further elution with 1050 ml of hexane gave 382 mg of recovered XXX. Continued elution with 450 ml of ether-hexane mixtures and 300 ml of ether gave 32 mg of a resinous material which appeared to be polymeric and was discarded.

Irradiation of 4,7a-Dimethyl-5(7aH)-indanone (XXX)

in Anhydrous Dioxane; Broad Spectrum Lamp

Compound XXX, 656 mg (0.0041 moles), was dissolved in ca 250 ml of freshly distilled anhydrous dioxane and irradiated with a 450 watt Hanovia high pressure arc. The reaction was followed by removing aliquots of the reaction mixture at regular intervals and analyzing these mixtures by vpc. At short reaction times, the tricyclic ketone XXXVI was the principal photoproduct but this was observed to be converted to another compound as irradiation was continued. After 120 min irradiation, the new compound accounted for 46 percent of the reaction mixture. Attempted chromatography on silica gel failed to separate the new compound from XXXVI and XXX. The new compound was purified by preparative vpc on a 10 foot SE-30 column, yielding 149 mg (22 percent) of a pale yellow oil identified as 4,4-dimethyl-tetrahydro- $\Delta^{6,7;8,9}$ -5-indanone (XXXVII). Compound XXXVII exhibited the following spectral properties:

uv max 335 m μ (ϵ 3,820); ir (CCl₄) 3.37, 3.49, 6.00 (conj C=O) and 6.12 (C=C) μ

nmr δ 6.86 (d, 1H, J=10.0 Hz), 5.79 (d, 1H, J=10.0 Hz), 1.76-2.75 (broad absorption, 6H), 1.16 (s, 6H); Mass spectrum (70 eV) m/e 162 (M⁺)

Anal C₁₁H₁₄O

Calcd: C, 81.44; H, 8.70

Found: C, 81.52; H, 8.68

Catalytic Hydrogenation of 4,4-Dimethyl-tetrahydro-

$\Delta^{6,9;8,9}$ -5-indanone (XXXVII)

Compound XXXVII, 102 mg (.000636 moles), was dissolved in ca 60 ml

of 95 percent ethanol, and 17 mg of 10 percent palladium on carbon was added. The mixture was placed on a Parr low pressure hydrogenation apparatus at 45 psig of hydrogen and shaken for 16 hrs. The catalyst was removed by filtration, and the solvents were removed in vacuo. The crude product was an oil, having a carbonyl absorption in the ir at $5.86\ \mu$ (lit. $5.86\ \mu$ (41)). The semicarbazone of this hydrogenation product was prepared and showed m.p. $203-6^{\circ}\text{C}$ (lit. $207-8^{\circ}\text{C}$ (41)).

Irradiation of 4,7a-Dimethyl-5(7aH)-indanone (XXX)

in 45 Percent Aqueous Acetic Acid

Compound XXX, 2.10 g (0.0124 moles), was dissolved in ca 350 ml of 45 percent aqueous acetic acid and irradiated for one hour with a 450 watt Hanovia high pressure mercury arc source. The solvents were removed in vacuo by azeotropic distillation with toluene. The crude oily photoproduct was placed on a column of 40 g of silica gel and eluted as follows.

Elution with 350 ml of hexane and 500 ml of 10 percent ether-hexane gave 679 mg (34 percent) of recovered XXX. Further elution with 800 ml of 10 percent ether-hexane gave 85 mg (3.3 percent) of a white crystalline solid identified as the rearranged hydroxy ketone acetate 3,7-dimethyl-7 acetoxy-5,6,7,7a-tetrahydro-2-(4H)-indenone (XXXVIII). Compound XXXVIII was purified by sublimation at high vacuum and exhibited the following properties:

m.p. $95-96^{\circ}\text{C}$; uv max $238\ \text{m}\mu$ ($\epsilon 7700$); ir (CHCl_3) 3.42 , 5.81 (ester C=O) 5.93 (conj C=O) and 6.10 (C=C) μ

nmr δ 1.40-3.26 (broad absorption, 9H), 1.93 (s, 3H), 1.42 (s, 3H)
1.20 (s, 3H)

Anal $C_{13}H_{18}O_3$

Calcd: C, 69.75 H, 8.11

Found: C, 69.51 H, 7.95

Continued elution with 600 ml of 25 percent ether-hexane, 1400 ml of 50 percent ether-hexane, and 1000 ml of ether gave 1.28 g (59 percent) of the rearranged hydroxy ketone 3,7-dimethyl-7-hydroxy-5,6,7,7a-tetrahydro-2(4H)-indenone (XXXIX). Compound XXXIX was purified by sublimation at high vacuum and had the properties reported below.

m.p. 59.5-60°C; uv max 242 m μ (ϵ 6,100); ir (CHCl₃) 2.69, 2.83
3.35, 5.91 (conj C=O), 6.08 (C=C) and 6.92 μ
nmr δ 1.46-2.92 (broad absorption, 10H), 1.43 (s, 3H), 0.79 (s, 3H);
mass spectrum (70 eV) m/e 180 (M⁺)

Anal $C_{11}H_{16}O_2$

Calcd: C, 73.30 H, 8.95

Found: C, 73.06 H, 8.67

Irradiation of 1,7a-Dimethyl-3a,7a-dihydro-3a,7-cyclo-

6(7H)-indanone (XXXVI) in 45 Percent Aqueous Acetic Acid

Compound XXXVI, 211 mg (0.0013 moles), was dissolved in ca 250 ml of 45 percent aqueous acetic acid and irradiated for 30 min with a 450 watt Hanovia high pressure mercury arc source. The solvents were concentrated by distillation at reduced pressure to ca 10 ml. The last 10 ml of solvent was removed by azeotropic evaporation with toluene in vacuo. The crude product

was placed on a column of four grams of silica gel. Elution with 150 ml of hexane, 300 ml of 10 percent ether-hexane, 200 ml of 25 percent ether-hexane, and 200 ml of 50 percent ether-hexane gave only trace amounts of oils which were discarded. Further elution with 300 ml of ether gave 144.6 mg of a clear oil which crystallized on standing overnight in the freezer. The crystals melted at 59-62°C and had an ir and nmr spectra identical in all respects to the 5/6-fused hydroxy ketone XXXIX. This represents a yield of 66 percent.

Irradiation of 6,7a-Dimethyl-5(7aH)-indanone (XXIX)

in 45 Percent Aqueous Acetic Acid

Compound XXIX, 523 mg (0.00323 moles) was dissolved in ca 250 ml of 45 percent aqueous acetic acid and irradiated with a 450 watt Hanovia high pressure mercury arc source for 105 min. The solvents were removed by azeotropic evaporation with toluene in vacuo, and the product was placed on a column of 10 g of silica gel. Elution with 300 ml of hexane followed by 300 ml of 10 percent ether-hexane gave 105 mg (22 percent) of recovered compound XXIX. Further elution with 300 ml of 25 percent ether-hexane and 1450 ml of 50 percent ether-hexane gave 140 mg (24 percent) of a compound tentatively identified as 6,7a-dimethyl-6-hydroxy-3,4,6,7-tetrahydro-3a,7-cyclo-5(7aH)-indanone (XL) and 248 mg (46 percent) of 1,7-dimethyl-7-hydroxy-5,6,7,7a-tetrahydro-2-(4H)-indanone, b.p. 90-95/0.1 mm Hg (bath temperature).

Compound XL exhibited the following spectral properties: uv, no maximum above 210 mμ; ir (CCl₄) 2.77, 2.92, 3.46, 3.49, and 5.79 (C=O) μ;

nmr, (60MHz) δ 4.06 (s, 1H), 1.42-2.96 (broad absorption, 7H), 2.49 (d, 1H, $J_{AB}=18\text{Hz}$), 2.21 (d, 1H, $J_{AB}=18\text{ Hz}$), 1.20 (s, 3H), 1.17 (s, 3H); nmr (100 MHz) verified $J_{AB}=18\text{ Hz}$. The exact mass of this compound was determined by mass spectrometry as 180.155 (Calcd. for compound XL:180.155).

Compound XLI exhibited the following properties: m.p. $70.5-71^{\circ}\text{C}$, uv $234\text{ m}\mu$ (ϵ 16,500), ir, (CCl_4) 2.77, 2.92, 5.84 (C=O), 6.13 (C=C) μ ; nmr; δ 5.81 (m, 1H), 1.50-3.39 (broad absorption, 9H), 1.30 (d, 3H, $J=7.5\text{Hz}$), 0.92 (s, 3H); mass spectrometry (70 eV) 180 (M⁺)

Anal $\text{C}_{11}\text{H}_{16}\text{O}_2$

Calcd: C, 73.30; H, 8.95

Found: C, 73.10; H, 8.96

Reaction of 5,7a-Dimethyl-3a,7a-dihydro-3a,7-cyclo-
6(7H)-indanone (XXXV) with Aqueous Acetic Acid

Compound XXXV, 750 mg (ca 70 percent pure: compound XXIX and a small amount of XXVI was present in this sample) (0.0046 moles) was dissolved in 300 ml of 45 percent aqueous acetic acid and stirred for about three hours. The solvents were removed in vacuo by azeotropic distillation with toluene. The resulting brown oily residue was placed on a column of 18 g of silica gel. Elution with 125 ml of hexane and 150 ml of 10 percent ether-hexane gave 172 mg of a mixture of XXXV and XXVI (ca 90 percent XXXV by vpc analysis on a 10 foot x 1/4 inch SE-30 Diatoport column, 180°C). Further elution with 150 ml of 10 percent ether-hexane and 450 ml 25 percent ether-hexane gave 194 mg of XXIX. Continued elution with 300 ml of 50 percent ether-hexane and 450 ml of ether gave 182 mg (23 percent) of 6,7a-dimethyl-6-hydroxy-3,4,6,7-tetrahydro-3a,

7-cyclo-5(7aH)-indanones. (XL)

Periodic Acid Oxidation of 6,7a-Dimethyl-6-hydroxy-

3,4,6,7-tetrahydro-3a,7-cyclo-5(7aH)-indanone (XL)

Compound XL, 87 mg (0.00048 moles) was dissolved in 50 ml of an ethereal solution of periodic acid containing ca 0.00048 moles of periodic acid and stirred for 14 hours. The solvents were removed in vacuo to yield 64 mg of an oil which had ir absorptions at 3.38, 3.40, 3.49, 5.73 and 5.87 μ and showed two singlets in the nmr at δ 1.28 and 1.38.

CHAPTER IV

DISCUSSION OF RESULTS

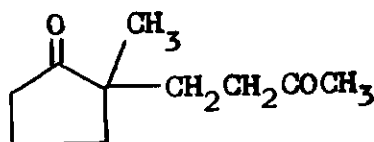
As mentioned in Chapter I, the primary objective of this research was to investigate the photochemical rearrangements of cross-conjugated cyclohexadienones related to indan. The first part of this discussion covers the synthesis of these dienones. The second and third parts of the discussion will respectively cover the results of the irradiations and mechanistic considerations involved.

The basic starting material for all of the dienones used was 2-methylcyclopentanone (XXII) which was readily synthesized by methylation and decarboxylation of 2-carbethoxycyclopentanone (31).

The parent unsubstituted indanone (XXIII) had previously been reported by deFeu, McQuillin and Robinson (27) and more recently by Ray and Gupta (32). Robinson's method of synthesis, involving condensation of 2-methylcyclopentanone (XXII) with the methiodide salt of 4-dimethylamino-2-butanone suffers from poor yield; attempts to reproduce this work in these laboratories gave erratic results (33). Ray's procedure, in which 2-methylcyclopentanone (XXII) was condensed with 4-chloro-2-butanone in the presence of sodamide, was not attempted.

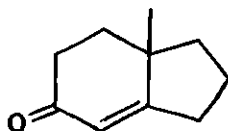
The general method of Ross and Levine, which has been used successfully for the synthesis of several naphthalenones (26) was employed. In this technique, 2-methylcyclopentanone was condensed with the appropriate vinyl

ketone using ethanolic potassium hydroxide as a catalyst and anhydrous ether as the solvent. Buchanan and McLay (34) reported that under these conditions 2-methylcyclopentanone condensed with methyl vinyl ketone to give the dione XXIV in unstated yield.

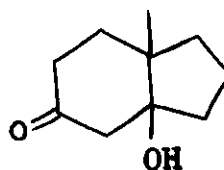


XXIV

In our hands, however, the condensation gave a three component mixture as analyzed by vapor phase chromatography. Infrared and nuclear magnetic resonance spectroscopy indicated that the mixture consisted of XXIV plus the ketol XXV and the desired enone XXIII in a ratio of about 2:1:2.



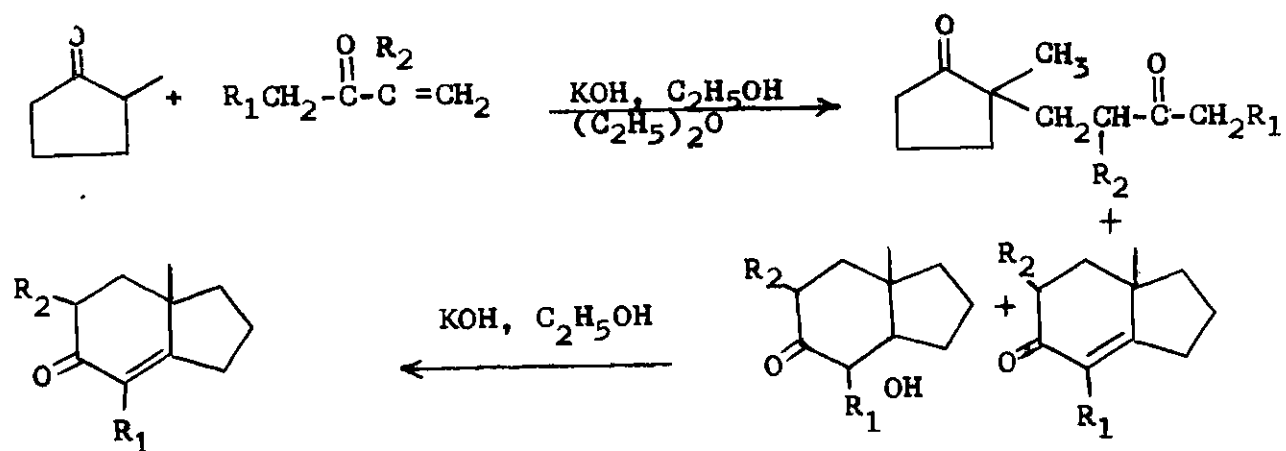
XXIII



XXV

Aqueous hydrochloric acid and piperidine both failed to convert the crude mixture to compound XXIII. The mixture was converted to XXIII in good yield with ethanolic potassium hydroxide.

This two step method, as outlined in Chart 4, proved to be a most satisfactory synthesis for the desired enones. It should be noted that it was necessary to run these reactions in a nitrogen atmosphere. Several attempts to condense



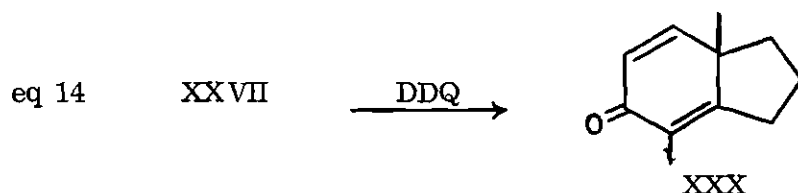
<u>Vinyl Ketone</u>	R_1	R_2	<u>Yield</u>	<u>Compound</u>
Methyl vinyl ketone	H	H	57	XXIII
Ethyl vinyl ketone	CH_3	H	47	XXVII
Methyl isopropenyl ketone	H	CH_3	33	XXVI

Chart 4. Syntheses of Some Dihydroindanones

2-methylcyclopentanone with methyl vinyl ketone in air gave extremely poor yields.

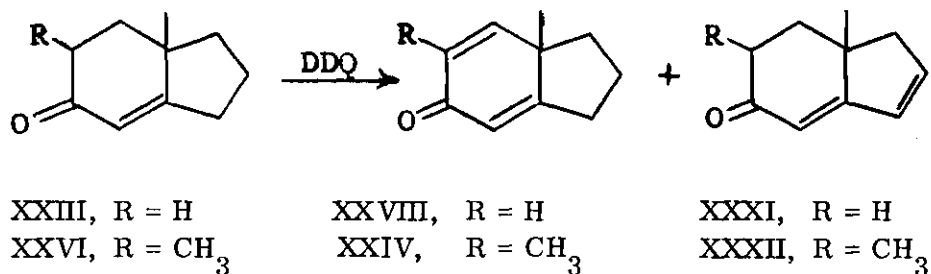
Compounds XXIII, XXVI, XXVII gave spectral data consistent with the assigned structures. Compounds XXVI and XXVII had not been synthesized previously and gave satisfactory analytical results.

In general, use of DDQ is the most convenient method for conversion of enones to cross-conjugated cyclohexadienones. Compound XXVII reacted cleanly with this reagent to give the desired dienone XXX in 60 percent yield (Equation 14).



Compounds XXIII and XXVI, however, reacted with DDQ to give what appeared to be, by ultraviolet and nmr spectroscopy, mixtures of the desired dienones XXVIII and XXIX respectively and the linear conjugated dienones XXXI and XXXII (Equation 15).

eq 15



Both XXIII and XXVI reacted with selenium dioxide under the conditions of Bloom (29) to give the desired cross-conjugated cyclohexadienones XXVIII and XXIX respectively. Spectral properties of the dienones XXVIII and XXIX are summarized in Table 1. The absorption for the C₄-H of compound XXVIII at δ 5.89 partially obscures the upfield component of the AB quartet for the C₆-H and C₇-H centered at δ 5.99.

The failure of Compounds XXIII and XXVI to cleanly form cross-conjugated cyclohexadienones with DDQ, and the observation that the desired cross-conjugated products XXVIII and XXIX respectively were formed on treatment with selenium dioxide can be explained in terms of the mechanisms of the two oxidations.

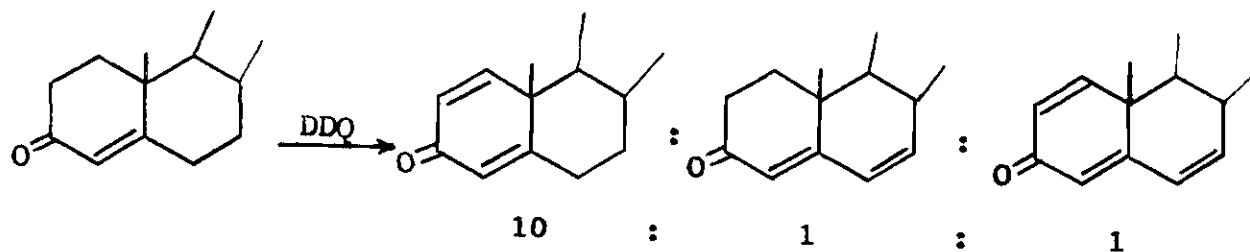
Ringold and Turner (35) found that in the absence of acid, androst-4-ene-3,17-dione reacted with DDQ in refluxing dioxane to give three products, the 1,4-dienone, 4,6-dienone and 1,4,6 trienone in ratio 10:1:1 (Equation 16).

Table 1. Spectral Properties of Simple 6/5 Fused
Cross Conjugated Cyclohexadienones

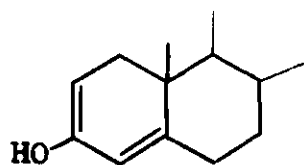
Compound	EtOH		
	$\lambda_{\text{max}}, \text{m}\mu$	ir*, μ	nmr, δ
XXVIII	244 (2a)	6.03, 6.12 (29)	7.02 (d, 1H, Jab=9.5 Hz)
	242 (obs)	6.03, 6.12 (observed)	5.99 (d of d, 1H, Jab=9.5 Hz Jax=2.0 H) 5.89 (m, 1H) 1.32-3.08 (broad absorption, 6H) 1.21 (s, 3H)
XXIX	244	5.97, 6.14	6.72 (q, 1H, J=1.5 Hz) 5.88 (t, 1H, J=1.8 Hz); 1.41-2.92 (6H) 1.79 (d, 3H, J=1.5 Hz); 1.18 (s, 3H)
XXX	243	6.01, 6.21	6.99 (d, 1H, J=9.5 Hz) 6.02 (d, 1H, J=9.5) 1.15-2.83 (6H) 1.72 (s, 3H); 1.17 (s, 3H)

* Only carbonyl and olefin absorptions are given. More complete spectra of compounds XXIX and XXX are given in Chapter II.

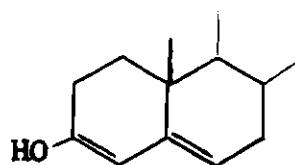
eq 16



In acid media, larger amounts of the 4,6-dienone were formed. It was postulated that the kinetic enol (XLII) forms in the absence of acid and undergoes C-1 hydride abstraction faster than the kinetic enol can equilibrate to the more thermodynamically stable enol (XLIII) which can undergo C-7 hydride abstraction.



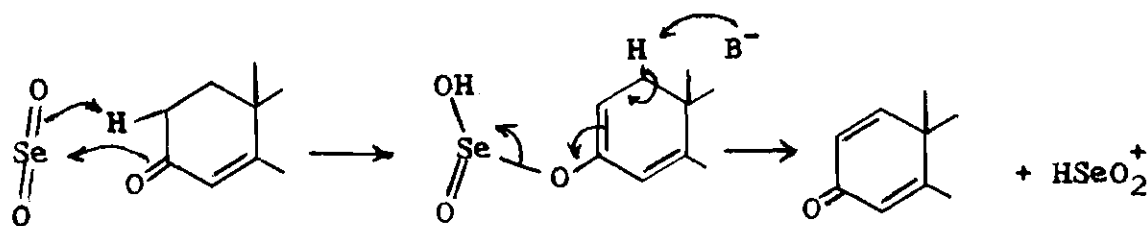
XLII



XLIII

Langbein (36a) and Corey (36b) studied the mechanism of the selenium dioxide dehydrogenation of ketones and found that the initial step in the mechanism involves coordination of the selenium with the carbonyl oxygen to yield a postulated intermediate selenite ester that can decompose to the desired cross-conjugated cyclohexadienone (Equation 17).

eq 17



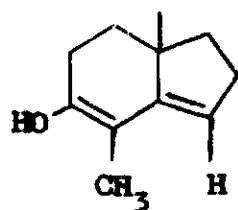
Evidence for the argument that the reaction does not proceed via the enol form is found in the observation that the rate increase is only about twofold when the solvent is changed from tert-butyl alcohol (catalysed by a trace of acetic acid) to 50 mole percent nitric acid in tert-butyl alcohol.

As previously stated, compounds XXIII and XXVI give mixtures of linear and cross-conjugated cyclohexadienones on treatment with DDQ.

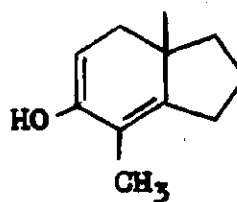
In the case of compound XXVI, the C-6 methyl may furnish some steric hindrance to the formation of the kinetic enol. The rate of formation of the thermodynamic enol may compete effectively with that of the kinetic enol. Additionally, this same methyl group could also furnish hindrance to C-7 hydride abstraction by DDQ. Kropp has reported that the naphthalenone analog of XXVI does not react with DDQ in refluxing dioxane (17).

The formation of the heteroannular dienol of compound XXIII must likewise be very rapid. This would explain the mixed products obtained.

Compound XXVII does react with DDQ to give the desired cross-conjugated dienone cleanly. A reason that the heteroannular dienol is not rapidly formed in this system may be that in the enol (XLIV) there would be an A¹⁽³⁾



XLIV



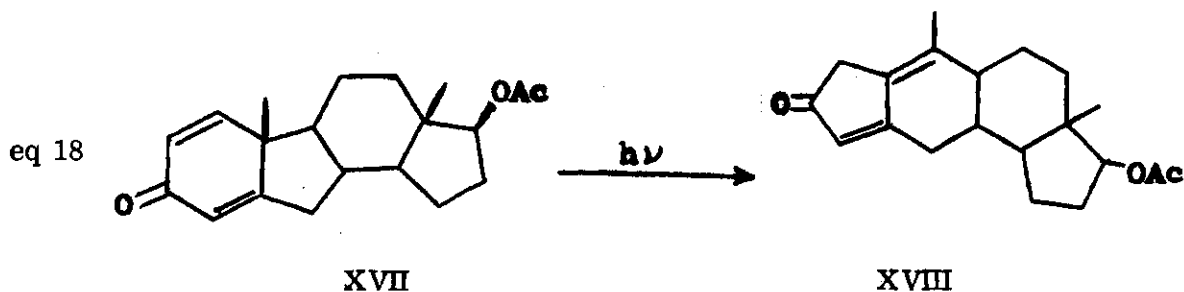
XLV

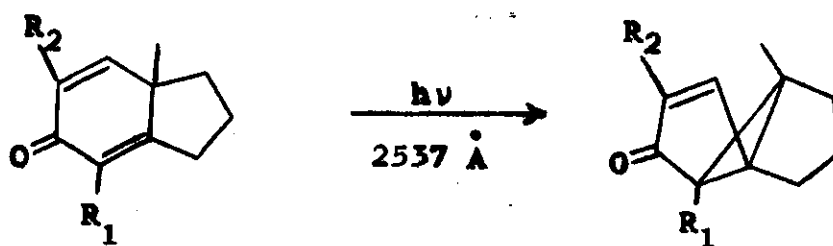
hydrogen-methyl interaction between the C-3 hydrogen and the C-4 methyl (37). Additionally the C-4 methyl may stabilize the homoannular dienol (XLV).

Compounds XXVIII, XXIX and XXX all gave tricyclic 5/3/5 lumiproductions on irradiation in anhydrous dioxane at $2537\overset{\text{O}}{\text{\AA}}$. Results of these irradiations are tabulated in Chart 4.

The spectral properties of the lumiproductions (XXXIII, XXXV and XXXVI) are quite similar to those of the lumiproductions derived from the analogous 6/6 fused systems. The spectral properties of both sets of compounds are tabulated in Chart 5.

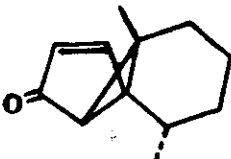

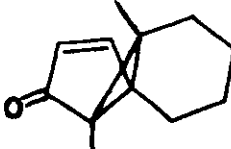
These results are quite surprising in light of the results of Jeger and co-workers (23) who reported that the dienone from B-nor-testosterone acetate (XVII) was converted to the linear conjugated dienone XVIII on irradiation at $2537\overset{\text{O}}{\text{\AA}}$ (Equation 18). This result was explained by the mechanism shown in Chart 2 (Chapter I).





<u>Dienone</u>	R_1	R_2	<u>Irradiation time, min.</u>	<u>Lumiproduet formed</u>	<u>Yield, percent</u>
XXVIII	H	H	75	XXXIII	Uncertain
XXIX	H	CH_3	90	XXXV	67
XXX	CH_3	H	120	XXXVI	38 (48 percent conversion)

Chart 5. Irradiation of 7a-Methyl-5(7aH)-indanones in Dioxane

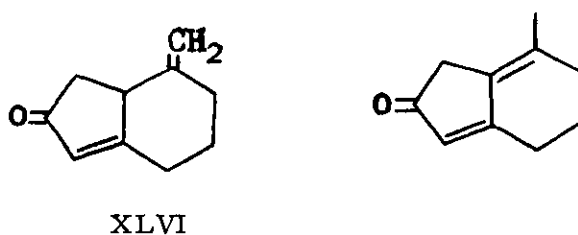
Compound	EtOH λ max, m μ	ir, μ *	nmr, δ
XXXIII	236 (ϵ 6300) 271 (ϵ 4200)	5.86	7.28 (d, 1H, J=5.5 Hz), 5.77 (d of d, $J_{AB}=5.5$, $J_{BX}=0.8$), 1.47-2.27 (m, 7H), 1.66 (s, 3H)
	236 (ϵ 6100)	5.92, 6.34	7.38 and 5.78 ($J_{AB}=5.5$ Hz, $J_{AX}=0.8$ Hz and $J_{BX}=1.1$ Hz); 1.24 (d, 3H, J=7.0 Hz); 1.18 (s, 3H) (ref 21)
XXXV	235 (ϵ 4660) 283 (ϵ 2120)	5.86	6.84 (m, 1H, 1.45-2.33 (m, 7H), 1.66 (d, 3H, J=1.5 Hz) 1.11 (s, 3H)
	234 (ϵ 5280) 270 (ϵ 1900)	5.92, 6.14	6.86 (m, 1H) 1.68 d, 1H, J=1.5, 1.12 (s, 3H) (ref 21)
XXXVI	247 (ϵ 4820) 274 (ϵ 2900)	5.88, 6.36	7.28 (d, 1H, J=5.5), 5.75 (d, 1H, J=5.5), 1.56-2.80 (m, 6H), 1.18 (s, 3H), 1.08 (s, 3H)
	240 (ϵ 4650)	5.92,	7.34 (d, 1H $J_{AB}=5.5$ Hz), 5.88 (d, 1H $J_{AB}=5.5$ Hz), 1.28 (s, 3H) 1.15 (s, 3H) (ref 17)

* Carbonyl and olefin stretching frequencies only

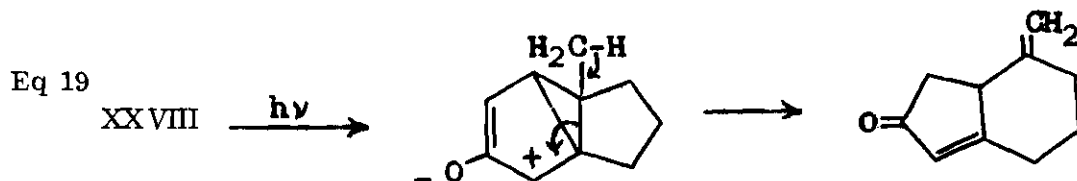
Chart 6. Spectral Properties of Some Lumiproducs

A second product (XXXIV), analogous to Jeger's linear dienone, was also formed on the irradiation of XXVIII. Examination of the reaction mixture by uv spectroscopy on completion of irradiation showed that a small amount of XXXIV was present ($\lambda_{\text{max}}^{\text{dioxane}}$ 288 m μ). When the reaction mixture was concentrated by removal of solvents in vacuo, the relative amount of XXXIV was increased several fold. Examination of the concentrated reaction mixture by nmr indicated that the ratio of XXXIII to XXXIV was ca 5:2.

A possible explanation for this phenomenon is that an intermediate photoketone that thermally isomerizes to XXXIV and has the same vpc retention time as XXXIII is formed. When large (50 to 75 μ l) samples of the crude concentrated reaction mixture were injected into the vpc, the relative amount of XXXIV seemed to increase, while the size of the peak attributed to XXXIII appeared to decrease. A possible structure for this unidentified photoketone is XLVI.



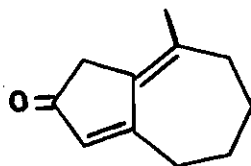
Compound XLVI could arise as shown in Equation 19.



The compound isolated by Jeger et al could likewise form through an *exo*-methylene intermediate analogous to XLVI.

The intermediacy of the lumiprodut (XXXIII) in the formation of the linear dienone (XXXIV) in either a thermal reaction or on a chromatography column was ruled out by two experiments. Heating a small sample of pure XXXIII for one hour at 100°C produced no change detectable by vpc. Allowing a pure sample of XXXIII to remain on a silica gel column for 14 hours likewise produced no change as detected by vpc.

A comparison of the spectral properties of compounds XVIII, XXXIV and the 5/7 fused heteroannular dienone XLVII (38) is given in Table 2.

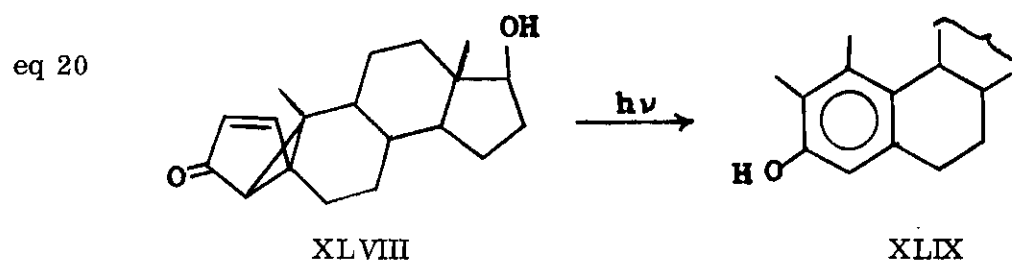


XLVII

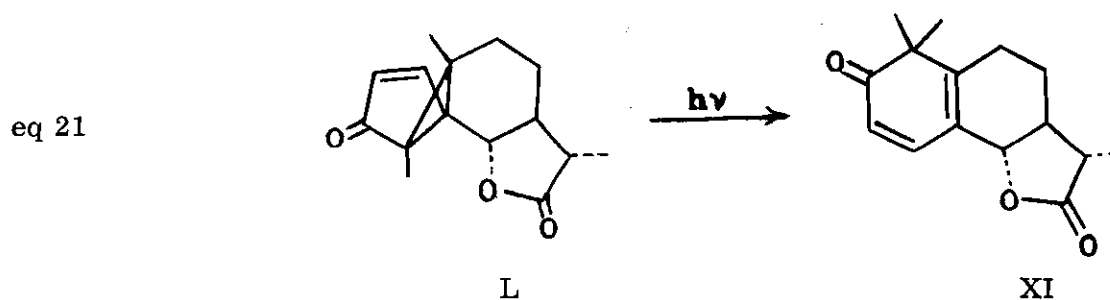
Table 2. Spectral Properties of Some Heteroannular Dienones

Compound	$\lambda_{\text{max}}^{\text{EtOH}}$	ir, μ	nmr, δ
XVIII (23)	299 (ϵ 14,500)	5.87, 5.96, 6.32	5.92 (s, 1H), 2.94 (s, 2H), 1.86 (s, 3H)
XXXIV	296 (ϵ 19,000)	5.86, 5.97, 6.31	5.61 (s, 1H), 2.70 (s, 2H), 1.53-2.90 (broad absorption, 6H) 1.81 (s, 3H)
XLVII (38)	300 (ϵ 10,900)	5.99, 6.40	5.86 (s, 1H), 2.83 (s, 2H) 1.85 (s, 3H)

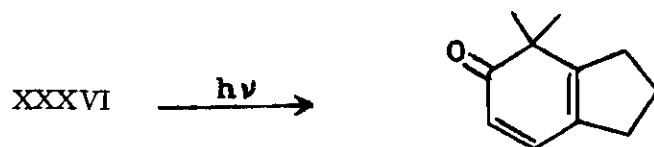
The lumiprodut derived from XXX is of special interest. On further irradiation with light greater than $3000 \overset{\text{O}}{\text{\AA}}$, most lumiproduts derived from bicyclic 6/6 dienones (eg XLVIII) give phenols (XLIX) (Equation 20) (39).



A notable exception to this general rule is the case of lumisantonin (L) which gives mazdasantonin (XI) on irradiation in inert media (Equation 21).



The strain induced by the lactone fused to the B-ring of lumisantonin is said to cause this abnormality (19). If strain is indeed the cause for the observed course of reaction, the lumiprodut (XXXVI) should form the linear dienone XXXVII on further irradiation.

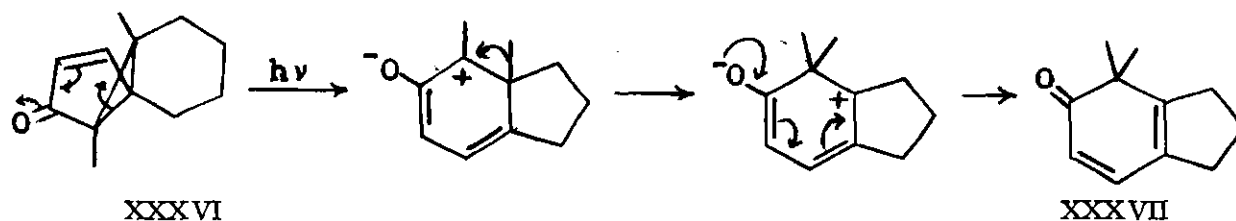


Irradiation of XXX with a 450 watt high pressure source in dioxane gave the lumiprodukt (XXXVI) which rearranged to a new compound, identified as XXXVII.

Compound XXXVII was hydrogenated to the known tetrahydro derivative which had $\lambda_{\max}^{\text{CCl}_4}$ 5.86 μ (C=O) (lit. $\lambda_{\max}^{\text{CCl}_4}$ 5.86 μ (41); semicarbazone, m.p. 206–9°C (lit. 207–8°C (41)).

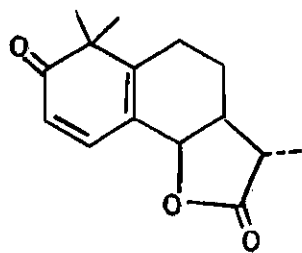
The mechanism of the conversion of XXXVI to XXXVII is quite probable similar to the lusisantonin-mazdasantonin conversion mechanism proposed by Fisch and Richards (20) and is given in Equation 23.

eq 23

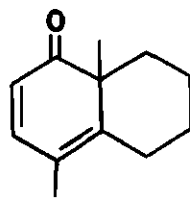


The more general formation of phenolic products is probably not observed in this case since formation of a spiro[5.3] intermediate would be required.

The ultraviolet spectral properties of Compound XXXVII, mazdasantonin (XI), 6-epi-mazdasantonin (XI a) and the homoannular dienone LI reported by Caine (40) are tabulated in Table 3.



XI a

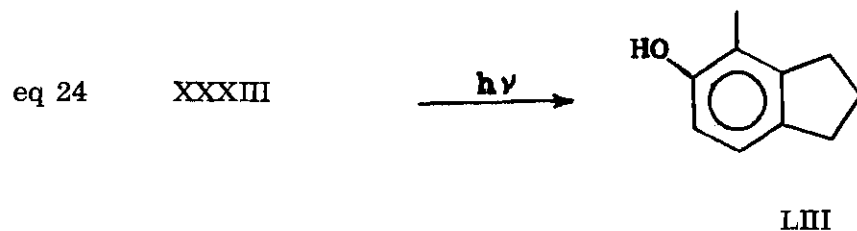


LI

Table 3. Ultraviolet Spectra of Some Homoannular Dienones

Compound	EtOH	ϵ
	$\lambda_{\text{max}}, \text{m}\mu$	
XXXVII	335	3820
XI	218	7700
XIa	308	
LI	328	3550

The lumiprodukt XXXIII should rearrange to the phenol LIII on extended irradiation (Equation 24).

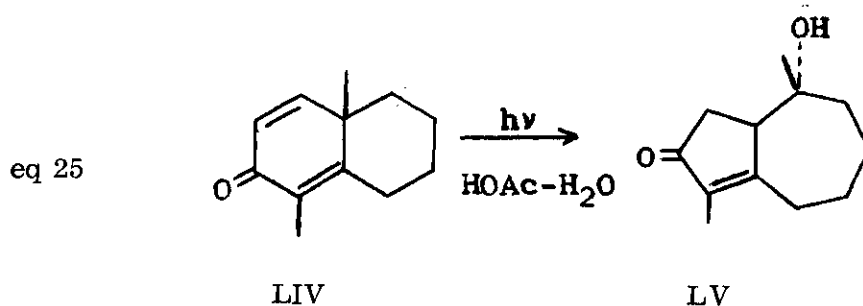


Attempted irradiation of both XXVII and its lumiprodukt (XXXIII) with a broad spectrum source gave only a resinous amber material from which no identifiable

compounds could be isolated.

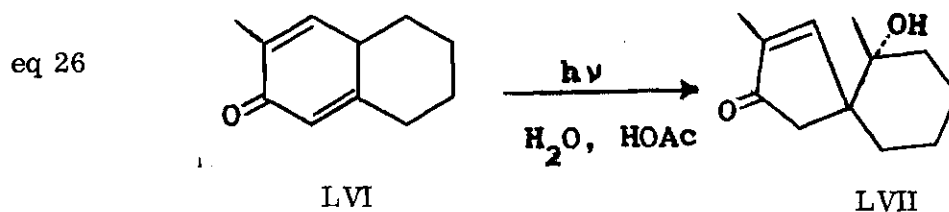
When compound XXXVI was dissolved in 45 percent aqueous acetic acid and irradiated with a broad spectrum high pressure mercury arc source, rearrangement to the 5/6 fused hydroxyketone XXXIX occurred. This was thought to be a dark reaction as no photochemical conversions of lumiproductions to analogous structures have been reported. In a later experiment, a small portion of the lumiproductions (XXXVI) was dissolved in 45 percent aqueous acetic acid and stirred in the dark. None of the 5/6 fused hydroxyketone (XXXIX) was formed in this reaction, indicating that the conversion of XXXVI to XXXIX is a new type of photochemical reaction.

As stated in Chapter I, bicyclic 6/6 fused cross-conjugated cyclohexadienones with a 4-methyl group rearrange cleanly to give 5/7 fused hydroxyketones on irradiation in aqueous acidic media. An example of this is the reaction reported independently by Caine and Dawson (42) and Kropp (43) in which the cyclohexadienone LIV rearranges cleanly to the perhydroazulene LV in 45 percent aqueous acetic acid (Equation 25).

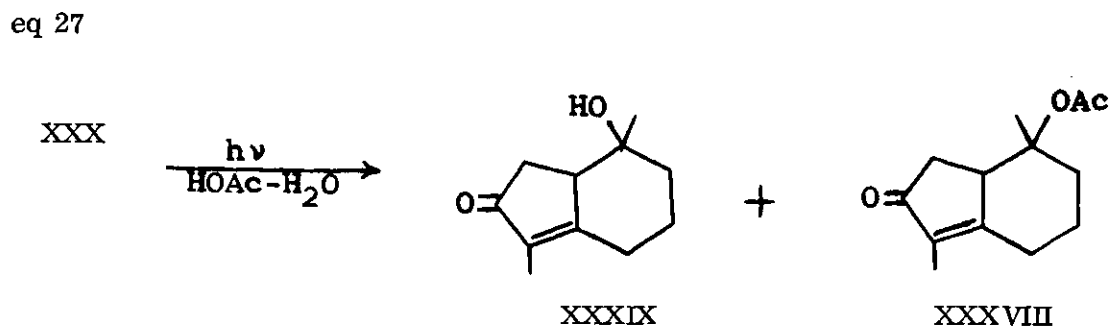


Bicyclic 6/6 fused cross-conjugated cyclohexadienones with a 2-methyl substituent have been shown to rearrange chiefly to spiro (4.5) hydroxyketones

on irradiation in aqueous acid media as in the conversion of LVI to LVII (Equation 26) (21).



On irradiation with a 450 watt high pressure mercury arc source, compound XXX gave the rearranged hydroxyketone XXXIX and, in trace amounts, the rearranged hydroxyketone acetate (XXXVIII) (Equation 27).



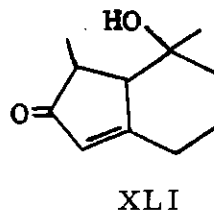
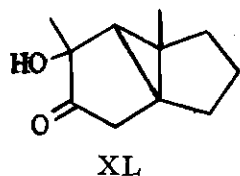
The rearrangement of XXX in aqueous acidic media is then exactly analogous to its naphthalenone counterpart. Compound XXXVIII arises by attack of acetic acid rather than the more nucleophilic water on the intermediate formed in the reaction. Spectral properties of compounds LV and XXXIX are compared in Table 4.

Table 4. Spectra of Rearranged Hydroxyketones

Compound	EtOH	ir, μ^*	nmr, δ
	$\lambda_{\text{max}}, m\mu$		
LV	243	6.17 5.95	7.55 (m) 0.91 (S)
XXXIX	242 (ϵ 6100)	5.91,	1.46-2.12 (broad absorption, 10H) δ 1.43 (s, 3H) δ 0.79 (3, 3H)

* Only carbonyl and olefin stretching frequencies are given. A more complete description of the ir of XXXIX is found in Chapter II.

Compound XXIX did not behave like its naphthalenone analog (LVI) upon irradiation in aqueous acidic media. As previously indicated, LVI rearranged to give the epimeric spiro hydroxyketones LVII upon irradiation in aqueous acetic acid (Equation 26). Compound XXIX, however, gave no spiro products under these conditions. Two hydroxyketones XL and XLI were formed in 24 and 48 per cent yields, respectively.



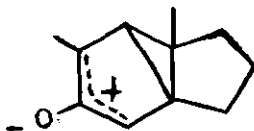
The structure assigned to XL is tentative. The assigned structure appears

to satisfy the spectral data given in Chapter III.

The broad singlet at low field was assigned to the hydroxyl proton. The AB quartet ($J_{\text{gem}} = -18$ Hz) was assigned to the C-4 hydrogens and the two singlets to the two methyl groups.

Additionally, this compound appeared to react with an ethereal solution of periodic acid. The product from this reaction was not identified, but was shown to be different from XL by ir and nmr spectroscopy.

A possible explanation for the formation of the 5/6 fused hydroxyketone (XLI) and the lack of formation of spiro products is that the 7-7a bond in the proposed intermediate (LVII) is exo to two five membered rings, rather than exo to one five and one six membered ring as in the case of the intermediate proposed for the 6/6 bicyclic systems. Since the 7-7a bond is exo to two five membered rings it would



LVII

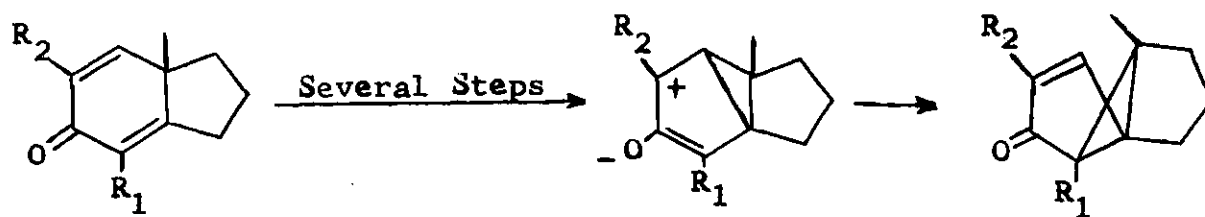
have more s character than the corresponding bond in the analogous intermediate. Conversely, the 3a-7a bond is in a five membered ring. This bond, then has a larger amount of p character than the corresponding bond in the intermediate proposed for naphthalenone systems, which would be in a six membered ring. The large amount of s character could make the 7-7a bond stronger than its analog in the intermediate 6/6 system. The large amount of p character in the 3a-7a

bond could make it weaker than its analog. Therefore, rearrangement by breaking the 3a-7a bond is to be favored energetically over rearrangement via rupture of the 7-7a bond, even though the methyl substituent does not favor this course of reaction. Compound XLI is the result of solvent attack at C-7a with displacement of the 3a-7a bond. The three membered ring in the proposed intermediate (LVII) is not effected in the formation of the tricyclic hydroxyketone (XL). Formation of this tricyclic product apparently occurs via reaction of the lumiprodukt (XXXV) with the solvent since a sample of XXXV rearranged to XL when stirred with 45 percent aqueous acetic acid at room temperature.

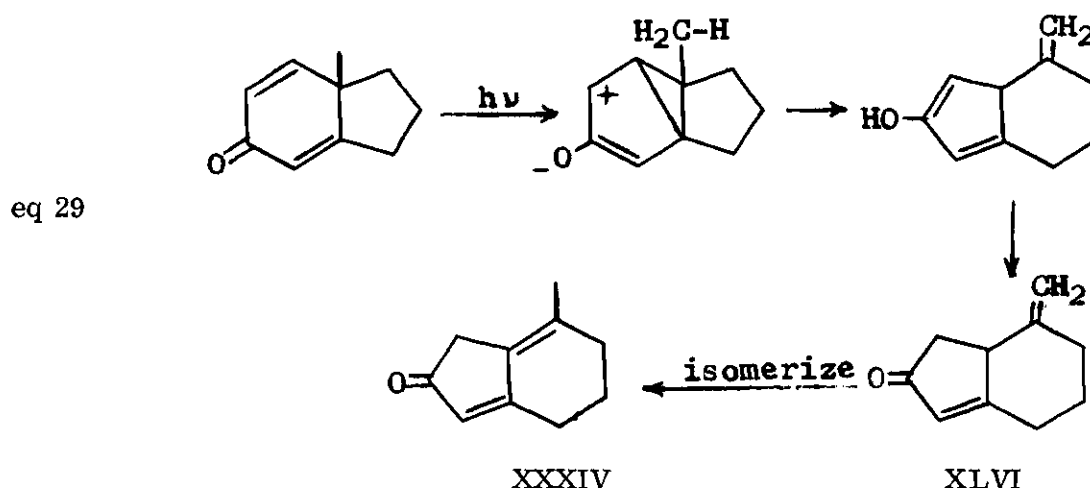
The data gathered on all of the compounds for which definite identification is claimed seems to indicate little doubt as to the correctness of the assigned structures. The details involved in the formation of these irradiation products is by no means completely elucidated.

The formation of the three lumiprodukt, Compounds XXXIII, XXXV, and XXXVI can be accommodated by use of the mesoionic intermediate postulated by Zimmerman and Schuster (12) as shown in Equation 28.

eq 28



The formation of the linearly conjugated dienone (XXXIV) and the steroidal analog reported by Jeger *et al* (23) can likewise be depicted as forming from the Zimmerman-Schuster intermediate either directly as shown in Chart 2 (Chapter I) or by formation of the exo-methylene isomer (XLVI) with concomitant isomerization of this compound to the observed product (Equation 29).



As previously stated, XXXIII did not rearrange on heating to 100°C for one hour or on standing on silica gel. This eliminates XXXIII as an intermediate in the formation of XXXIV.

Irradiation of XXX in 45 percent aqueous acetic acid gives the 5/6 fused hydroxyketone (XXXIX) and the acetate of this hydroxyketone (XXXVIII). This course of rearrangement is analogous to that of the similarly substituted naphthalenone (LIV) (42, 43). Both of these results can be rationalized in terms of solvent attack on the Zimmerman-Schuster intermediate as outlined in Chapter I. Since the lumiprodukt (XXXVI) derived from XXX appears to rearrange to the

hydroxyketone, XXXIX, under the reaction conditions used for the irradiation of XXX, the intermediacy of XXXVI cannot be ruled out.

Unlike XXX, compound XXIX does not react in a manner analogous to its naphthalenone counterpart (21). The formation of the 5/6 fused hydroxyketone (XLI) can readily be rationalized in terms of the Zimmerman-Schuster intermediate. As previously stated, dark reaction of XXXV with aqueous acetic acid gives XL, the other hydroxyketone formed on irradiation of XXIX.

CHAPTER V

CONCLUSIONS

7-a-Methyl-5(7aH)-indanone and its 4- and 6-methyl derivatives were synthesized and irradiated in various media.

The previous postulation (23) that the 5/3/5 fused ring system is too strained to form is incorrect. All three indanones give 5/3/5 fused photoketones on irradiation at $2537 \overset{\text{O}}{\text{\AA}}$ in dioxane.

The effect of A-ring methyl substituents is somewhat different in the indanone case than in the naphthalenone systems. A C-4 methyl substituent in either class of compounds gives only a rearranged fused hydroxyketone on irradiation in aqueous acetic acid. A methyl group at C-6 in the indanone system does not, however, direct the rearrangement to form spiro hydroxyketones.

The use of mesoionic species has successfully been employed in the past to rationalize the results of cyclohexadienone rearrangements. The invocation of these hypothetical intermediates can be carried over to the indanone systems studied.

CHAPTER VI

RECOMMENDATIONS

The details of the irradiation of Compound XXVIII, which appears to form both a lumipproduct (XXXIII) and another product, the linear dienone XXXIV should be more clearly elucidated. Attempts to define the intermediate involved in the formation of XXXIV should be made.

The structure of Compound XL should be definitely proven. If the tentatively assigned structure is correct, it would represent the first successful trapping of the proposed mesoionic intermediate.

A systematic study of filters and quenchers on the cyclohexadienone rearrangement might give valuable insight into the detailed mechanism of the reaction.

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